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## THE DEVELOPMENT OF THE HUMAN VERUMONTANUM


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*(From the James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, Md.)*


Our knowledge regarding the origin and more particularly the development and structural formation of the verumontanum is far from complete. In studying the literature one finds numerous references to the development of the Wolffian ducts and to the gross changes of the Müllerian ducts in their transformation to form the prostatic utricle or sinus pocularis. Beyond the mere recognition of Müller's tubercle or Müller's hillock on the dorsal surface of the urogenital sinus, however, there are practically no recorded observations on the growth and notably the developing glandular structure of the verumontanum. Accurate studies begin only with adult life.

The notation of the occurrence of a raised prominence on the floor of the posterior urethra in connection with the development of the Wolffian and Müllerian ducts was probably first made by Müller. Felix,[1] in his monograph on the Development of the Urinogenital Organs, in Keibel and Mall's System of Embryology, states: "The two excretory ducts remain close together and the region in which they open becomes raised up into a hillock and projects into the lumen of the urethra; this hillock we shall term Müller's hillock." This structure, in its later stages containing the sinus pocularis (fused Müllerian ducts of the female), the lower ends of the paired Wolffian ducts with their openings, together with various glandular tubules and inter-tubular stroma comes to form the verumontanum of later embryonic and of adult life.

Rudinger[2] and Henle[3] among the earlier writers described the gross picture of the veru quite at length. Concerning the prostatic utricle or sinus pocularis much has been written. Morgagni[4] first called attention to this structure contained within the veru and later Albinus,[5] Schlichting[6] and particularly Weber,[7] discussed in some detail its formation and especially the analogy between it and the uterus of the female.

Among the present-day writers the work of Rytina[8] on the histology and gross anatomy of the adult verumontanum is the most complete and comprehensive. Lowsley[9] in his studies on the development of the human prostate gland only briefly mentions the changing morphology of the verumontanum.

The material for this study was obtained in part from the Embryological Collection of the Carnegie Institute and in part from the Obstetrical Service and from the Pathological Department of The Johns Hopkins Hospital. In all eight human embryos were studied varying in age from the thirteenth week of fœtal life until birth. The age of each was determined according to the table and classification of measurements in Keibel and Mall's[10] System of Embryology. The specimens were embedded in paraffine and serial sections were made through the genito-urinary tract of each specimen from the urachus to the anterior urethra. These were cut in varying thickness—6 $\mu$ and 15 $\mu$ in the younger and 40 $\mu$ in the older specimens. The sections were stained in hæmatoxylin

and eosin and every section was saved for study. The measurements of the various structures were made by means of a micrometer eye-piece for the lateral diameters and for the perpendicular height by counting the several sections, each of which was of a known thickness.

### Fœtus 80.3 mm. Long (CR), 13 Weeks Old

(No. 768c, Carnegie Collection)

Just below the internal vesical sphincter at a level where the proximal end of the prostatic utricle is first encountered the floor of the urethra is practically flat, while the lumen of the urethra as a whole is oval with the greatest diameter from left to right. The utricle is first found .7 mm. below the urethral floor as an elliptical cavity, viewed in cross-section, with its long diameter extending dorso-ventrally situated midway between the common ejaculatory ducts. These three structures, utricle and ejaculatory ducts, are surrounded by a mass of undifferentiated mesenchymatous cells which is somewhat poorly defined and blends without notable differentiation with the kindred cells going to form the intertubular prostatic tissue and the urethral walls themselves. The blood-vessels at this time occupy for the most part a position along the lateral margins of the cell mass and between it and the prostatic intertubular substance.

A few sections below this picture the mid-portion of the urethral floor shows a slight mid-line elevation with a consequent furrow at the base on either side. This furrow of elevation carries with it the mucous lining of the urethra composed of three layers of epithelial cells and below the undifferentiated mesenchymatous tissue going to form the urethral walls and the intertubular substance of the prostate. At this level there are no tubules of the middle lobe of the prostate demonstrable. As further sections are studied in order along the course of the posterior urethra an additional elevation is encountered on either side of the one noted above, lifting the urethral mucous membrane and underlying mesenchyme into two ridges resembling the one just described, although it is much smaller.

At the time of encountering these additional striæ of elevation there are several tubules of the middle lobe of the prostate noted situated midway between the first described elevation of the urethra and the ejaculatory ducts. During this progress through the sections the ejaculatory ducts have notably diminished in size and become practically round while the utricle has enlarged until now its diameter is twice that of the ejaculatory ducts and is pear-shaped or triangular in cross-section with its greatest width toward the dorsal surface of the prostate. The entire three structures in their course have come to occupy a position about the center of the prostatic tissue and have seemingly pushed the middle lobe tubules upward, well toward the urethral floor, where they are seen to open on either side of the middle elevation. At this point the middle and lateral elevations of the urethral floor merge into one rounded or half-moon-shaped structure composed of undifferentiated mesenchymatous tissue covered with the mucous lining of the urethra (which consists of several layers) and enclosing at its rather broad base the prostatic utricle and ejaculatory ducts. These in their upward slanting course have now reached the urethral level or base of the verumontanum. From here the structures take an upward slanting direction and the ejaculatory ducts finally open simultaneously on the sides of the verumontanum about its middle portion well up towards its summit. The utricle continues as a closed canal for only a few sections beyond the openings of the ejaculatory ducts where it ends as a blind pouch .1 mm. below the mucous surface of the verumontanum. The veru continues for about .3 mm. beyond the last vestige of the utricle and finally fades away in three slim elevated ridges or striæ as in its origin from the floor of the urethra above.

The veru measures about .7 mm. in length in this specimen from its origin in the striæ just outside the internal sphincter to its end in the small similar folds extending down toward the membranous urethra. Its height is .4 mm. at the most prominent portion which is above and anterior to the openings of the ejaculatory ducts and where the ducts and utricle first reach the base of the veru on their upward slanting course through this organ. The width of the veru at its widest point, which is also at the site of greatest height, is .7 mm., making it of equal length and breadth at this stage. The prostatic utricle extends as a hollow tube lined with mucous cells one or two layers deep for a little over .4 mm. coursing through the prostate gland in an upward slanting direction.

The cavity of the utricle is somewhat cigar-shaped and on cross-section tends to be oval, measuring about ⅛ by 1/10 mm. in diameter. At this stage the veru is made up of a mass of undifferentiated mesenchymatous cells budding forth from the mid-ventral portion of the urethral floor and pushing the urethral mucous membrane before it. Its cells cannot be differentiated from those forming the intertubular substance of the prostate itself. There is no evidence of any tubular elements in the verumontanum as yet, but above are a few tubules of the middle lobe of the prostate which may be seen entering the urethra along the prostatic furrows sometime before the openings of the ejaculatory ducts are encountered.

The walls of the ejaculatory ducts are composed of undifferentiated mesenchymatous cells, which are as yet not unlike those going to form the substance of the veru itself. At the openings of the ejaculatory ducts into the urethra there is no suggestion of any change in the arrangement of the cells, but here the mucous lining of each duct is approximated so that the lumina of the ducts are filled in. The cells going to form the veru even at this state are more closely packed and take the stain more deeply than those of the intertubular substance of any of the prostatic lobes, a fact indicating embryologically that they are perhaps a little older or were laid down a little earlier than the prostatic stroma.

### Fœtus 105 mm. Long (CR), 14 Weeks Old

(No. 1358e, Carnegie Collection)

The three striæ arising from the urethral floor entering into the formation of the verumontanum above are less marked in this specimen. In fact, the middle elevation is the only one that can be readily recognized. At the first level of its identification, however, the tubules of the middle and two lateral lobes of the prostate and also of the anterior lobe are well formed. The urethra in this specimen is cone-shaped with its base corresponding to the floor of the urethra. The veru at this time is well formed and at its upper portion near the internal sphincter is an almost pedunculated organ in cross-section. Its upper surface is covered with a mucous membrane having several layers and continuous with that lining the urethra. Over the veru, however, this mucous covering is quite irregular in outline, dipping down in places to form notable pits and in some places forming a series of pockets which become shut off from the lumen of the urethra and appear as definite tubules of the outer portion of the verumontanum.

This irregularity is first noted at the tip of the veru, but in the succeeding sections it is seen to extend well down on either side to the prostatic furrows. The prostatic utricle is first observed at the base or urethral level of the veru as a slit-like aperture with its long diameter extending dorso-ventrally, while on either side are situated the common ejaculatory ducts. The utricle is lined with a several-celled layer of mucous cells in all respects similar to those lining the ejaculatory ducts.

About the utricle and ducts the mesenchymatous cells are a little more closely packed and somewhat more deeply staining than in other portions of the veru. The utricle and ducts continue an upward slanting course through the substance of the

veru and the ducts finally open into the urethra on either lateral aspect of the veru very near its summit. The utricle continues for a few sections beyond these openings and then ends as a blind pocket nearly .5 mm. below the mucous membrane of the veru. The utricle is about .6 mm. long in this specimen and .3 mm. in its greatest diameter, which is dorso-ventrally, while its walls are approximated throughout its entire course. From all points the utricle is essentially only a verual organ in this specimen at this stage. The verumontanum measures approximately .7 mm. long and .7 mm. in diameter in its widest portion, while its highest point is 1.3 mm. from the urethral floor.

The composition of the veru is still for the most part undifferentiated mesenchyme, while the walls of the ducts and utricle show simply a more close approximation of cells and as yet no definite musculature. The peripheral tubules are present, seven on the left side and four on the right, formed from infoldings of the mucous covering.

An interesting finding in this specimen shows the tip of the veru in its lower third securely attached to the roof or dorsal aspect of the urethra. This condition is apparently rare if not constituting a real anomaly, as it has not been observed in any of the other specimens studied.

### FŒTUS 130 MM. LONG (CR), 16 WEEKS OLD

(No. 1018, Carnegie Collection)

As soon as the internal sphincter is passed the longitudinal striæ which merge to form the upper surface of the veru are encountered. The middle fold is first noted, being somewhat longer than the other two situated one on either side of it. At the level where the striæ are first observed there are present the tubules of the middle and two lateral lobes of the prostate, but none of the anterior are seen. The middle fold increases in size in its course down the urethra and finally the lateral folds become a part of it. At the level where the veru may be said to begin the ejaculatory ducts are .5 mm. below the urethral floor with a few middle-lobe tubules between these two points. The urethra is somewhat star-shaped with the veru projecting well into its lumen. The irregularity of the mucosa covering the veru is noted again in this specimen forming well-defined pits, though this is not so marked as in the previous specimen.

The utricle is first encountered just below the urethral level and at the base of the veru as a somewhat irregular opening, but in general circular in outline measuring about .1 mm. in diameter situated .25 mm. below the surface of the veru. It is lined with mucous cells one or two layers deep. Immediately beneath the mucosa covering the veru the previously undifferentiated cells have now become more specialized and here form a well-defined covering over this organ of an early stroma-like sheath. Within this sheath are included the utricle and the two ejaculatory ducts which are still surrounded by a mass of clearly undifferentiated mesenchymatous cells. This stroma-like sheath can easily be traced down to the somewhat similar intertubular structure of the prostate gland with which its fibers are closely intermingled. Within this stroma are here encountered for the first time several tubules or gland acini which come to lie along the sides of the now well-formed verumontanum. In tracing these structures through the veru it is seen that they first occupied a position as a part of the sub-urethral portion of the prostate middle lobe and have seemingly been pushed upward to occupy their new position by the upward growth of the verumontanum. At this time also is noted the definite fibrous elements in and about the walls of the utricle and ejaculatory ducts. All tubules observed open into the urethra along the sides of the veru and in no instance have any tubules of prostatic origin been observed opening into either the utricle or ejaculatory ducts.

Through the veru the ducts and utricle pursue an upward slanting course and all assume an elliptical outline in cross-section. This is brought about to a considerable extent by the pressure from either side by the formation of the stroma-like sheath and the growth of several tubules within this enclosure. The ejaculatory ducts first occupy a position below the utricle at the upper level of the veru just beneath the termination of the superior striæ. In their course downward, however, they become separated and, before the mid-verual portion is reached, come to occupy a position on either side of the utricle. At this time the utricle appears as a longitudinal slit lined with mucous membrane and its walls approximated. It measures at this time .4 mm. in its dorso-ventral diameter.

Continuing their course upward the ducts decrease in size and finally, about the mid-portion of the veru, open through the sides of this organ very near its tip into the urethra. The utricle continues for a few sections beyond the openings of the ejaculatory ducts where it ends as a blind pouch .05 mm. beneath the mucous membrane of the veru. The utricle measures a little over .6 mm. in length in this specimen and is sword-shaped with its walls approximated and the greatest diameter extending dorso-ventrally. After the openings of the ejaculatory ducts are passed and beyond the utricle the verumontanum becomes a highly tubular organ. This is caused by the tubules of the middle lobe (prostate) seemingly pressing upward, so that some five or six of them have come to occupy a position in the veru giving it a decided honeycombed appearance in cross-section. After this has continued for some distance, these tubules of prostatic origin disappear and over the lower or inferior third of the organ only the infoldings arising from invaginations of the mucous covering are seen, while the extreme inferior portion of the veru has no tubular elements. As in the earlier specimen the veru gradually fades away into three or possibly four small but definite striæ of elevation, which are observed decreasing in prominence as they are traced down the prostatic urethra toward the external sphincter. The veru measures 1.25 mm. long and .6 mm. wide in its greatest diameter, while its greatest height is .4 mm. at the level of the openings of the ejaculatory ducts.

### FŒTUS 171.4 MM. LONG (CR), 19 WEEKS OLD

(No. 1049, Carnegie Collection)

The utricle is first encountered in this specimen fairly high up, before there is any indication of the formation of the veru or before even the superior striæ are noticed. It is observed as an irregular star-like cavity lined with a mucous membrane of several layers and with its walls approximated. It measures .4 mm. by .1 mm. in diameter in cross-section, the greatest width extending dorso-ventrally, and lies .5 mm. below the urethral floor. Just dorsal and on either side of it are situated the ejaculatory ducts which are about the same size as the utricle, but with their walls well dilated. Between the utricle and urethral mucosa are observed several tubules (six or seven of the middle prostatic lobe, the sub-urethral portion). Also in their respective areas about the urethra are noted the tubules of the anterior, and the two lateral lobes, and also those of the posterior lobe.

The intertubular substance of the prostate is here well defined as an unmistakable stroma. A few undifferentiated mesenchymatous cells still remain grouped about the utricle, but about the ejaculatory ducts the differentiation into a muscular coat is observed. On either side of the mid-line the urethral floor with its mucosa is slightly elevated for a short distance appearing as two striæ. The middle fold described in the three previous specimens is here lacking. These two striæ are soon lost in the general elevation of the mid-urethral floor by the pushing up of the veru. The stroma-like sheath marking the boundaries of the veru, mentioned in the previous specimen, is here still more strikingly shown, and within this the undifferentiated mesenchyme still persists, yet in the region about the utricle it has begun to take on a somewhat stroma-like aspect.

In following the ejaculatory ducts through the prostate they decrease in size as in the previous specimen and become elliptical in outline, their long diameter extending dorso-ventrally. The mucosa over the superior third of the veru is still somewhat irregular with moderate invaginations and pit formation. This irregularity is not so marked as in the specimens at 14 and 16 weeks, but is still quite evident. In their course through the veru the ejaculatory ducts and utricle pursue an upward, slanting path and the ducts finally open simultaneously in the mid-portion of the veru well up toward its tip. Even at this time there is scarcely to be noted a definite musculature to their walls, but merely a more deeply staining layer of cells which somewhat resemble stroma cells. The utricle extends only a few sections beyond the openings of the ejaculatory ducts where it ends as a blind pocket .05 mm. below the mucous membrane covering the veru. The utricle measures 1.2 mm. long in this specimen and runs as a sword-like canal with its walls for the most part approximated.

Beyond the openings of the ejaculatory ducts and the distal portion of the utricle the veru is made up very largely of tubular elements having their origin from the sub-urethral portion of the middle lobe. These with a relatively small amount of stroma and only a slightly irregular mucous membrane go to make up the organ. All tubules open on either side of the veru along its inferior third directly into the urethra. Beyond the openings of the ejaculatory ducts the tubules are more numerous, but in the superior or upper portion those of prostatic origin can be definitely made out. After the region of the tubules is passed the intertubular stroma of the veru continues for a short distance down the urethra as a central ridge and is finally lost in the floor of the urethra. The lateral inferior striæ were not found in this specimen. The veru at this time measures 2.5 mm. in length, .5 mm. in height and .9 mm. in width along its greatest diameter.

### Fœtus 178 mm. Long (CR), 21 Weeks Old

(No. 1171, Carnegie Collection)

In this specimen the superior striæ are present and well developed. The middle elevation is most prominent and on either side are two definite folds resembling to a considerable degree the picture seen in the previous specimen. The folds are covered with mucous membrane three- or four-cell layers deep, while the underlying stroma is seen extending well into each elevation. The utricle is first encountered .5 mm. beneath the superior striæ before the real urethral elevation of the veru is observed. It exists as a circular cavity, .4 mm. in diameter, situated just above the common ejaculatory ducts, which are here circular cavities .3 mm. in diameter. Both between the ejaculatory ducts and utricle on the one side and between the utricle and urethra on the other are observed several tubules of the prostatic middle lobe.

The superior striæ continue over the upper third of the veru in this specimen and are finally lost in the irregularities of the mucous membrane. This irregularity, as in the earlier specimens, has now become quite characteristic of the upper third of the veru. It is traced into pits and in the deeper portion to definite tubule formation. These tubules arising from the urethral mucosa occupy a position about the extreme periphery of the organ. The glands from the prostate (middle lobe), previously mentioned as lying above the utricle, are in the progress of the upward slanting course of the utricle and ejaculatory ducts gradually pushed upward until they become gland tubules of the veru itself. Here they occupy a position along the lateral walls of the organ beneath those tubules derived from the infolding urethral mucous membrane. These deeper tubules derived from the prostatic middle lobe finally open into the urethra along the lateral walls of the veru itself.

In the course through the veru, after the superior third of the organ is traversed, the utricle becomes much smaller and its lateral walls become approximated with the ejaculatory ducts situated on either side of it. All three structures are at this level elliptical in outline with the greatest diameter extending dorso-ventrally. Without further notable change the ejaculatory ducts continue their upward slanting path and finally open up on either side of the veru well up toward its tip. The walls of the ejaculatory ducts are in this specimen well defined throughout and the changing mesenchymatous cells which make up their walls are well observed by their elliptical shape and their more densely staining properties. The utricle continues as a closed canal a few sections beyond the openings of the ejaculatory ducts and there ends as a blind pocket .1 mm. below the mucous membrane covering the veru.

The utricle is cigar-shaped in this specimen and measures about 1.4 mm. in length. Below or inferior to the openings of the ejaculatory ducts the veru is made up of a few tubules having their origin from the prostatic middle lobe. These are here few in number (about five or six) and soon end by opening into the urethra along the sloping sides of the veru. The remainder of the veru is made up entirely of stroma having a mucous covering similar to the urethra itself. In tracing the veru down toward the membranous urethra it is seen to fade away in three striæ or folds which soon decrease to the level of the urethra. The veru measures 1.4 mm. long, .7 mm. high and 1 mm. in width at its widest point.

### Fœtus 221 mm. Long (CR), 25 Weeks Old

(No. 1172, Carnegie Collection)

Along the superior or upper portion of the urethra the striæ which merge to form the veru are clearly delineated as three well-marked folds. The middle elevation is the most prominent, but in all three the basal stroma extends well into the substance of the folds as a series of conical peaks. The mucous covering is here, as in the previous specimens, several layers thick and along the sides of the veru the indentations and pit-formation are well defined. In certain areas tubule formation from the invaginating mucous membrane covering is readily recognized. These tubules occupy the periphery of the organ. Beneath these structures are scattered the tubules of the sub-urethral portion of the middle lobe of the prostate which have been pushed upward to occupy a position in the substance of the veru itself.

The utricle when first encountered occupies a position entirely within the veru as an elliptical cavity .6 mm. below the surface of the urethra and measures .5 mm. by .3 mm. in diameter. The ejaculatory ducts at this level occupy a position dorsal and to either side of the utricle as irregular, somewhat star-shaped cavities lined with mucous membrane. The stroma at this stage is very prominent in the structure of the veru, surrounding all tubules and forming a well-defined capsule about the utricle and ejaculatory ducts. Within this capsule there still remains a small amount of poorly differentiated mesenchyme, but that entering into the formation of the walls of the ducts and utricle has very nearly the appearance observed at birth.

In this course through the veru the utricle and ejaculatory ducts become considerably elongated or elliptical in cross-section and all three structures finally come to lie parallel with their long axes extending dorso-ventrally. At this time is noted for the first time an evagination and pit-formation from the walls of the utricle and to a very slight extent from those of the ejaculatory ducts also. This irregularity of their mucous lining gives these structures a definitely pocketed appearance in cross-section. A little beyond the level of this irregularity of their lining the ejaculatory ducts are seen to open on the sides of the urethra well up toward its tip. Their mouths are wide open with no suggestion of any sphincteric fibers at their orifices. The utricle extends a few sections beyond the openings of the ejaculatory ducts, but

there ends as a blind pouch .05 mm. beneath the mucous covering of the veru.

In this specimen is observed the pointed evagination of the ventral surface of the utricle toward the urethral lumen, directing its subsequent path of opening into the urethra. The utricle measures .5 mm. in length by .1 mm. in diameter at its greatest width and is confined entirely as a closed cavity within the veru. Beyond the openings of the ejaculatory ducts the veru is made up of several tubules of prostatic origin, which open along the sides of the urethra. These are surrounded by an abundance of intertubular stroma which is supplied with numerous blood-vessels. After the tubules are passed, the stroma with its rich blood supply makes up the entire verual elevation. The veru finally diminishes into three slight but definite folds, the inferior striæ, which gradually reach the urethral level toward the membranous urethra. The veru measures at this time 2 mm. long, 1 mm. high and 1.7 mm. wide.

### FŒTUS 276 MM. LONG (CR), 31 WEEKS OLD

(No. 7, Obstetrical Service of The Johns Hopkins Hospital)

The three superior longitudinal striæ are encountered at their beginning just below the internal sphincter in this specimen. They are covered with several layers of mucous membrane and, as in the previous specimen, the stroma extends well up into each elevation. Close beneath the striæ are several tubules of the middle prostatic lobe which later appear in the veru itself, well separated from the other middle lobe tubules. In following the sections down through the prostatic urethra the superior striæ are soon lost in the general elevation of the veru, which here is composed of numerous tubular nests closely bound around with stroma. All of the above-mentioned tubules open along the sides and a few at the summit of the veru.

The utricle first appears as a circular cavity 2.5 mm. below the surface of the veru and is .3 mm. in diameter. It is situated between the ejaculatory ducts which are quite irregular in outline and are approximately half the size of the utricle itself. The superior or upper third of the veru is composed very largely of the tubular elements derived from the infolding mucous membrane covering the veru, and its ventral surface is above extremely irregular owing to this infolding and pit-formation of the invaginating mucosa. In its course through the prostate the utricle increases in size and becomes irregular while the ejaculatory ducts on either side rapidly diminish in diameter and tend to become circular in outline.

When first observed the utricle and ejaculatory ducts are clearly walled off within a very definite stroma capsule and this persists about these structures during their course through the prostate gland. The sub-verual structures become thinned out in this specimen and the veru and utricle seem to approach each other by a thinning out of the intermediate tissue more than by a course through the prostate. At this level the few middle-lobe tubules, which eventually become a part of the verual gland tissue, are easily recognized and appear just above the utricle and are literally pushed up by it to their new position in the veru. The peripheral verual tubes from their origin from the infolding of the urethral mucosa are here well separated from the tubules of prostatic origin by a well-defined area of stromal tissue.

In tracing the varied structures through the veru the utricle is seen to become quite irregular in outline and in places almost star-shaped in cross-section. The evaginations from its main walls to form tubules are few, less numerous than in the preceding specimen, and are located for the most part between the utricle and ejaculatory ducts. All the structures finally open spontaneously into the posterior urethra, the utricle at the summit of the veru in the mid-line and the ejaculatory ducts on either side of the opening of the utricle. The utricle gives an almost double-duct appearance at this level by its great irregularity, possibly of significance from its origin from the paired Müllerian ducts of the female. About the openings of the ejaculatory ducts there is no evidence of any isolated fibers that might have a sphincteric action. Both orifices are free and gaping.

The opening of the utricle extends several sections further than the openings of the ejaculatory ducts. The utricle in this specimen is 3.5 mm. long. Beyond the duct openings and utricle the veru is composed of several lateral tubules of prostatic origin which soon open into the urethra through the mucous membrane of the veru. The remainder of the veru is made up of a dense stroma which is well supplied with blood-vessels. The inferior fourth of the veru is practically free from tubules of any type. The veru finally ends by decreasing into four ridges of elevation, the inferior striæ, which are lost in the floor of the urethra. The veru is 4.25 mm. long, .3 mm. high and 1.4 mm. wide at its greatest diameter.

### FŒTUS 338 MM. LONG (CR), AT BIRTH

(No. 8, Pathological Department of The Johns Hopkins Hospital)

As in the preceding specimens, the floor of the prostatic urethra in its upper portion presents essentially the same three elevations previously termed the superior striæ. The middle elevation is here the largest and all three have their origin soon after the last of the sphincteric fibers are passed. Each is covered with mucous membrane several cell layers deep, below which is the stroma extending well up into each elevation. Even at the level of the superior striæ the irregularity of the mucous covering is present and beneath the surface the definite tubules of the veru arising from this infolding or pit-formation is well demonstrated. The tubules of the middle prostatic lobe at this time are situated somewhat deeply beneath the urethral floor just above the irregular ejaculatory ducts and well separated from the first-mentioned tubules by a rather thick layer of stroma tissue.

In their course down the urethra the superior striæ soon lose their identity and become fused with the middle elevation, which then becomes the upper portion of the verumontanum. At this level the prostatic utricle is first encountered as a somewhat irregular circular aperture .2 mm. in diameter, lined with mucous membrane several cell layers deep, surrounded by numerous strands of loosely packed stroma. Beyond this is the more definite stroma capsule which contains the tubules of mucous membrane origin, some three or four on each side situated along the lateral margins of the veru. In its path through the veru the utricle becomes quite irregular, its mucous lining evaginating well into the adjacent stroma to form well-defined tubules, all of which empty into the utricle itself. The outer series of verual tubules of mucous membrane origin all empty into the prostatic urethra along the sides of the veru. At this level, the superior or upper third of the organ, the tubules of true prostatic origin (middle lobe) have not taken a place in the substance of the veru itself.

In the following sections the ejaculatory ducts are traced upward through the substance of the prostate, gradually becoming smaller, although still maintaining their rather marked irregularity of outline. In their upward course they are observed literally pushing up into the substance of the veru several tubules of prostatic origin. These later become pushed to either side of the veru and finally open up into the prostatic urethra on either side of the veru. At this level the tubules of mucous membrane origin have practically all disappeared, for they occupy for the most part only the superior third of the veru. Traversing the substance of the veru the outline of the utricle becomes more and more convoluted and its ensuing tubule formation becomes more marked so that at the level of its opening into the posterior urethra there is a veritable nest of tubules emptying into its lumen for the most part along the mid-line but to some extent also along its lateral

walls. The utricle opens into the urethra before the ejaculatory ducts and while the latter structures are still elliptical lumina on either side of the utricle lying a little less than .3 mm. below the urethral floor. From this picture the ejaculatory ducts pursue a rapid course upward toward the tip of the veru and finally open on the upper lateral walls of the organ on either side of the opening of the utricle. The utricle measures .3 mm. long and, although very irregular, tends to be sword-shaped and measures 1 mm. by .2 mm. in diameter.

At this level and in the succeeding slides the tubules of prostatic origin become more numerous and practically comprise the entire veru except for the few supporting strands of intertubular stroma. This picture continues for only about the third quarter length of the veru, after which a mass of stroma tissue comprises the remaining or last quarter length of the organ with only a rare tubule opening along its lateral margin. Finally, the veru fades away into three rather ill-defined elevations or striæ, which eventually become lost as they approach the level of the urethral floor in the direction of the external sphincter. The veru in this specimen is nearly 4 mm. long, 1 mm. high and 1.5 mm. wide in its greatest width.

## SUMMARY

(1) At the thirteenth week of fœtal life the verumontanum is merely a rounded elevation arising from the posterior urethral floor. It is composed of undifferentiated mesenchymatous cells and covered with mucous membrane. Three striæ merge above to form its elevation and the same number are encountered below at its termination. It has no tubular elements and measures .7 mm. in height and the same in breadth at its widest portion. It contains the prostatic utricle and the terminal portions of the ejaculatory ducts.

(2) By the fourteenth week definite glandular tubules of the veru have appeared, arising from invaginations of its mucous covering and occupying a definite position about the periphery of the organ. These tubules open into the posterior urethra. The prostatic utricle is contained entirely within the veru in this specimen.

(3) A second group of tubules of the veru appear by the sixteenth week. These are prostatic in origin, arising from the suburethral portion of the middle lobe. They occupy a position just below the outer strata of peripheral tubules and all open into the urethra along the middle third of the veru.

(4) The nineteenth week of fœtal life brings no material change in the character of the elements entering into the formation of the veru other than observed in the preceding specimens. The tubules of prostatic origin are, however, more numerous.

(5) At the twenty-fifth week the peripheral tubules arising from the invaginating mucous membrane and also the middle strata tubules of prostatic origin are readily identified. In addition irregularities of the walls of the prostatic utricle and to some extent of the ejaculatory ducts are observed, with tubule-formation from the evaginating lining of the utricle.

(6) The utricle opens into the posterior urethra at the summit of the veru between the twenty-fifth and thirty-first week. At the later date the three groups of tubules entering into the formation of the veru are clearly identified.

(7) At birth the veru measures 4 mm. long, 1 mm. high and 1.5 mm. in width. It is a highly glandular organ and the three sets of tubules, (a) those about the upper portion and periphery arising from the invaginating urethral mucosa, (b) those situated in the middle and lower portion arising from the prostatic middle lobe, and (c) those about the utricle arising from the evaginating mucous lining of the utricle are easily recognized. It contains also the terminal portions of the ejaculatory ducts and the prostatic utricle.

My thanks are due Dr. Hugh H. Young, director of the James Buchanan Brady Urological Institute, for the unlimited laboratory privileges extended; to Dr. George L. Streeter, of the Embryological Department of the Carnegie Institution of Washington, for the generous supply of material, and to Dr. Charles W. Bethune, of the Sisters' Hospital, Buffalo, for his painstaking care in making the photomicrographs.

## BIBLIOGRAPHY

1. Felix: Human Embryology. Keibel and Mall, 1912, Vol. 2, p. 752.

2. Rüdinger: Zur Anatomie der Prostata des Uterus Masculinus und der Ductus Ejaculatorii. Festschrift des Aerztl. Vereines, München, 1883, 47-67.

3. Henle: Handbuch der Systematischen Anatomie des Menschen. Braunschweig, 1866.

4. Morgagni: Adversaria Anat., LV, Anat. IV, Animad. 3.

5. Albinus: Annotat. Acad. IV, Tab. III, Fig. 3, p. 25.

6. Schlichting: Syphilidos Mnemosynon Criticum. Amst., 1646.

7. Weber: Annotationes Anatom. et Physiol. Programm zu D. E. Kratzachmar's Disput. Inaug. Circa Lineamenta Physiologiæ Morborum, Leipzig, 1836. Zusätze zur Lehre vor Baue und die Verrichtungen der Geschlechtsorgane, 1846.

8. Rytina: The Radical Removal of the Verumontanum. Jour. A. M. A., 1915, LXIV, p. 45. The Verumontanum, with Special Reference to the Sinus Pocularis: Its Anatomy, Histology and Physiology. The Jour. of Urology, 1917, I, No. 2, p. 299.

9. Lowsley: The Development of the Human Prostate Gland. With Reference to the Development of other Structures at the Neck of the Bladder. Amer. Jour. Anat., 1912, XIII, No. 3, p. 299.

10. Keibel and Mall: Human Embryology, 1912, Vol. I, p. 180.

## DESCRIPTION OF PLATES

Fig. 1.—Spec. No. 768c, Carnegie Collection. Fœtus 80.3 mm. long, 13 weeks old. Transverse section through the upper limit of the verumontanum. A. Central superior stria. B. Tubules of the prostate gland (middle lobe).

Fig. 2.—Spec. No. 768c, Carnegie Collection. Fœtus 80.3 mm. long, 13 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts opening into the prostatic urethra. No inherent glandular tubules are noted at this stage.

Fig. 3.—Spec. No. 1358e, Carnegie Collection. Fœtus 105 mm. long, 14 weeks old. Transverse section through the upper portion of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Early invagination of the mucous covering to form the peripheral tubules.

Fig. 4.—Spec. No. 1358e, Carnegie Collection. Fœtus 105 mm. long, 14 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Fibrous strands firmly attaching the tip of the veru to the roof of the urethra (an anomaly). D. Peripheral gland tubules of mucous membrane origin.

Fig. 5.—Spec. No. 1018, Carnegie Collection. Fœtus 130 mm. long, 16 weeks old. Transverse section through the upper portion

FIG. 1.

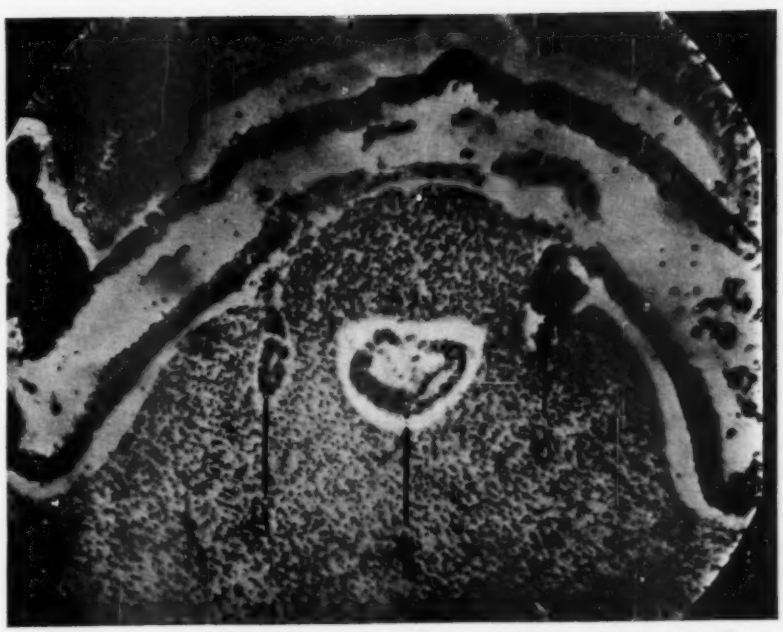


FIG. 2.

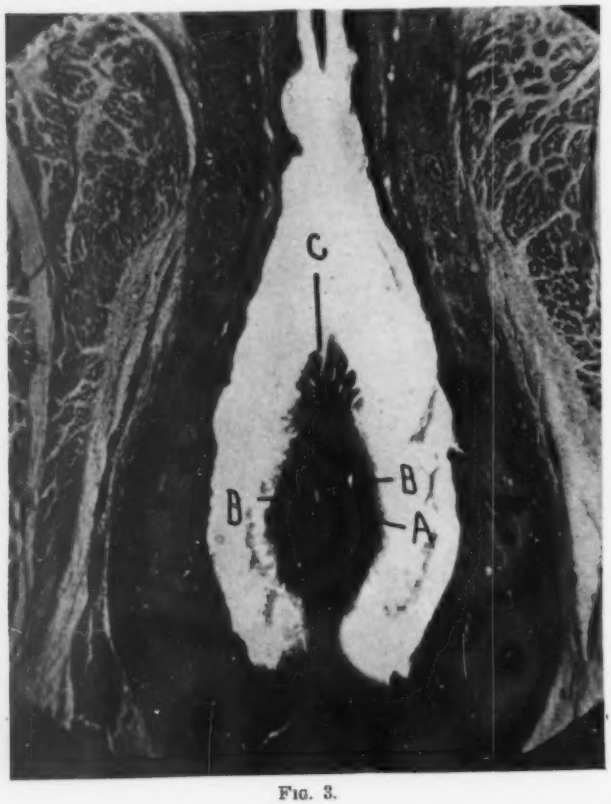



FIG. 3.

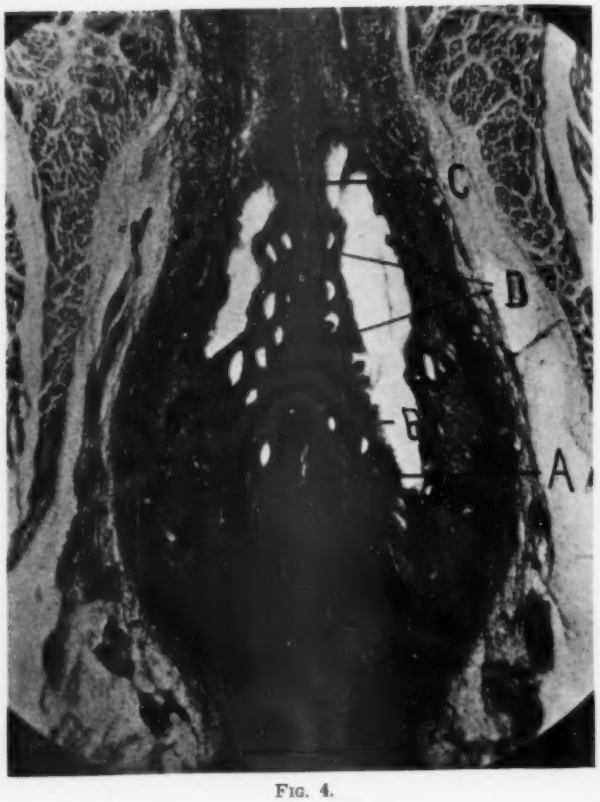



FIG. 4.

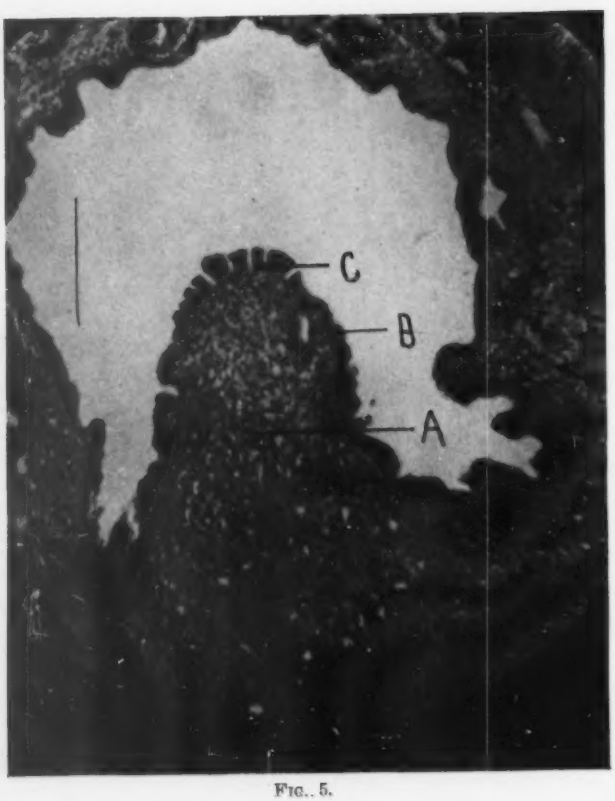



FIG. 5.

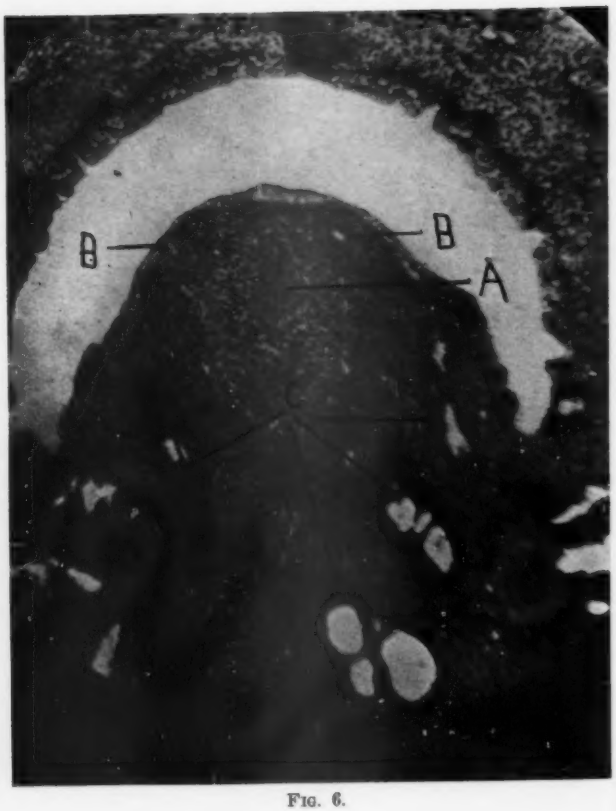



FIG. 6.

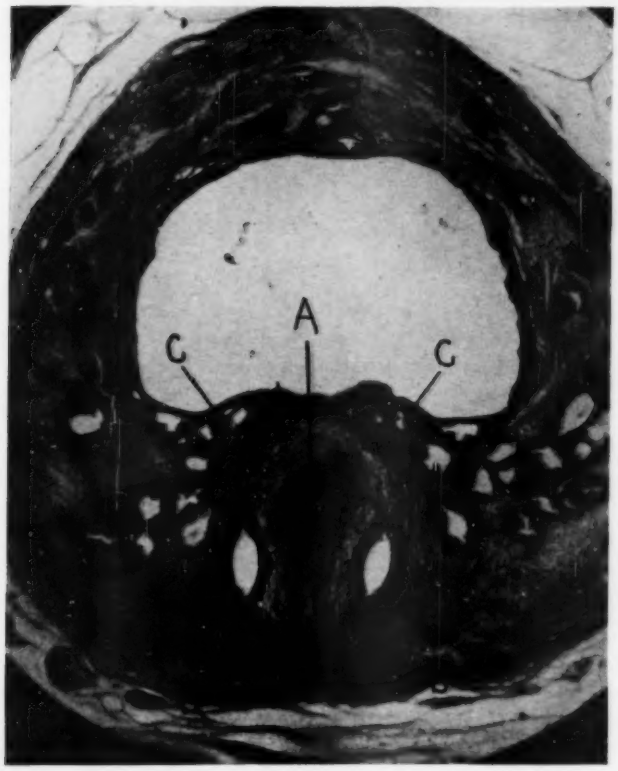



FIG. 7.

FIG. 8.

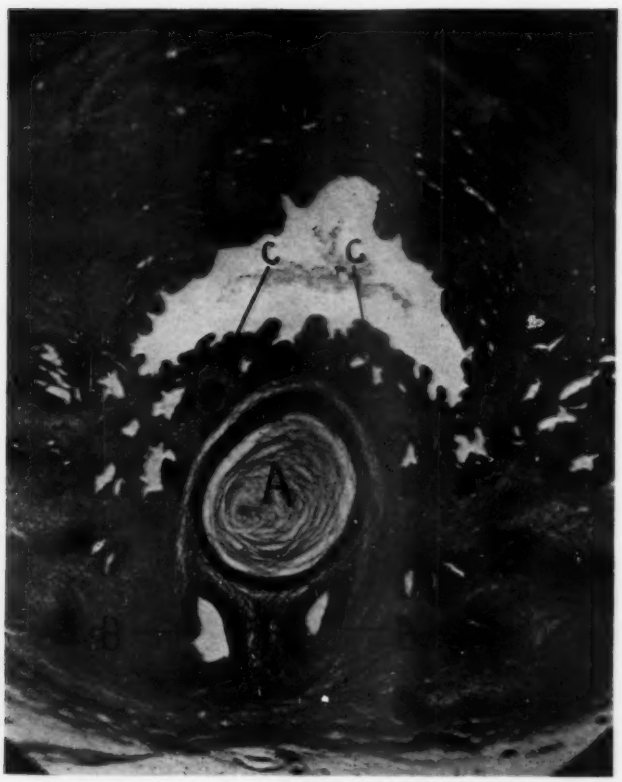



FIG. 9.

FIG. 10.

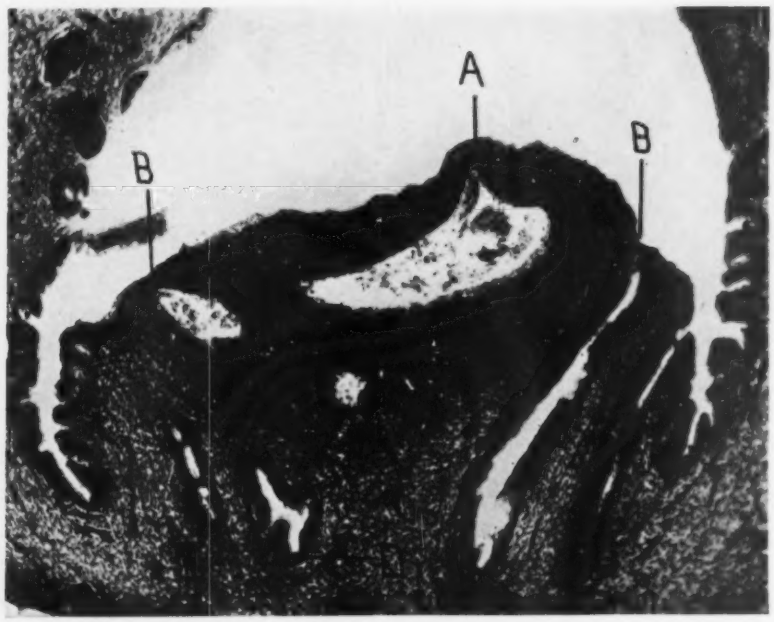



FIG. 12.

FIG. 11.

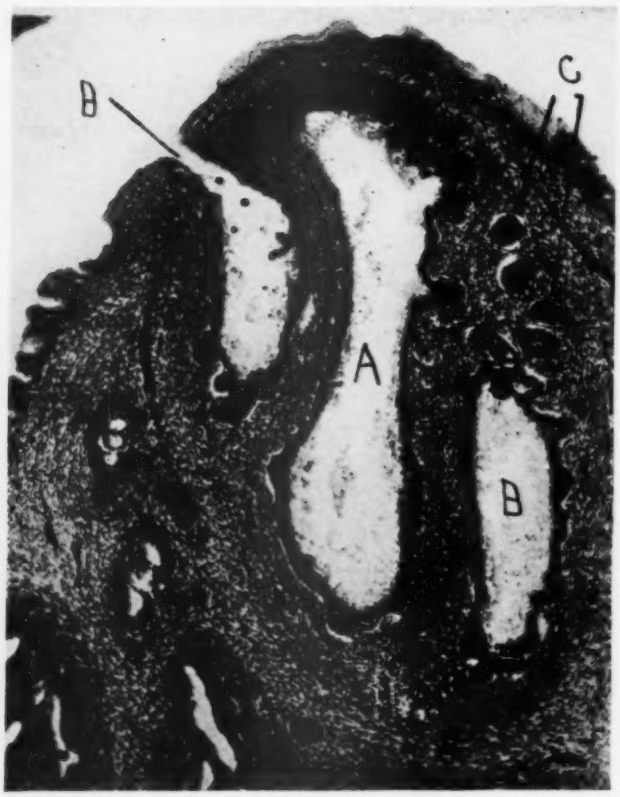



FIG. 13.

FIG. 14.

FIG. 15.

FIG. 16.

of the verumontanum. A. Undifferentiated mesenchyme of the veru. B. Peripheral tubules of mucous membrane origin. C. Pitting of the mucous covering to form tubules.

FIG. 6.—Spec. No. 1018, Carnegie Collection. Fœtus 130 mm. long, 16 weeks old. Transverse section through the lower third of the verumontanum. A. Prostatic utricle. B. Opening of the common ejaculatory ducts into the urethra. C. Gland tubules of prostatic origin (middle lobe) entering into the base and subperipheral portion of the veru.

FIG. 7.—Spec. No. 1049, Carnegie Collection. Fœtus 171.4 mm. long, 19 weeks old. Transverse section through the upper portion of the verumontanum. A. Prostatic utricle surrounded by a beginning stroma-like sheath. B. Common ejaculatory ducts. C. Gland tubules of mucous membrane origin.

FIG. 8.—Spec. No. 1049, Carnegie Collection. Fœtus 171.4 mm. long, 19 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Gland tubules of prostatic origin (middle lobe).

FIG. 9.—Spec. No. 1171, Carnegie Collection. Fœtus 178 mm. long, 21 weeks old. Transverse section through the upper portion of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Gland tubules of mucous membrane origin.

FIG. 10.—Spec. No. 1171, Carnegie Collection. Fœtus 178 mm. long, 21 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Gland tubules of mucous membrane origin. D. Gland tubules of prostatic origin (middle lobe).

FIG. 11.—Spec. No. 1172, Carnegie Collection. Fœtus 221 mm. long, 25 weeks old. Transverse section through the tip of the verumontanum. A. Prostatic utricle showing the irregularity of its lining membrane. B. Common ejaculatory ducts showing the irregularity of their walls. C. Gland tubules of mucous membrane origin.

FIG. 12.—Spec. No. 1172, Carnegie Collection. Fœtus 221 mm. long, 25 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle pointing its subsequent path of opening into the urethra. B. Common ejaculatory ducts. C. Gland tubules of utricular origin, formed from the evagination of the walls of the utricle. D. Gland tubules of prostatic origin.

FIG. 13.—Spec. No. 7, J. H. Hosp. Obstet. Service. Fœtus 276 mm. long, 31 weeks old. Transverse section through the upper portion of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Gland tubules of mucous membrane origin. D. Gland tubules of utricular origin.

FIG. 14.—Spec. No. 7, J. H. Hosp. Obstet. Service. Fœtus 276 mm. long, 31 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle opening into the urethra. B. Openings of the common ejaculatory ducts. C. Opening of a gland tubule of prostatic origin. D. Gland tubule of utricular origin, later opening into the prostatic utricle.

FIG. 15.—Spec. No. 8, J. H. Hosp. Path. Service. Fœtus 338 mm. long, at birth. Transverse section through the tip of the verumontanum. A. Opening of the prostatic utricle into the urethra with tubules entering it in the mid-line. B. Common ejaculatory ducts. C. Gland tubules of utricular origin. D. Gland tubules of prostatic origin (middle lobe). E. Tubule of mucous membrane origin.

FIG. 16.—Spec. No. 8, J. H. Hosp. Path. Service. Fœtus 338 mm. long, at birth. Transverse section through the lower portion of the verumontanum beyond the openings of the utricle and ejaculatory ducts. A. Openings of peripheral gland tubules of mucous membrane origin. B. Gland tubules of prostatic origin (middle lobe).

# ELECTROMYOGRAPHIC STUDIES OF CLONUS

By STANLEY COBB

*(From the Neurological Laboratory of the Henry Phipps Psychiatric Clinic, The Johns Hopkins Hospital)*

Clonus has been studied graphically by many investigators, but their results have not been uniform because mechanical methods were relied on until the introduction of electromyography. In the present work a few cases were studied intensively by means of the string galvanometer and the results seem to show that clonus gives a typical electromyogram, the details of which perhaps throw light on the nature of clonus. Beginning slowly, the periods between contractions soon shorten to a constant length, and this periodicity then varies not at all with fatigue, and only slightly with change of muscular tension. Clonus was kept up for half an hour in one case. In different individuals the average length of these periods varies only by a few hundredths of a second, the shortest being .12 second and the longest .17 second. From the theoretical standpoint the coincidence of this rate of clonus with the rate of other organic tremors brings to mind interesting speculations in regard to the nature of intrinsic neuro-muscular rhythms.

## LITERATURE

The study of clonus by graphic methods dates as far back as 1880, when Alexander James [10] recorded the contractions mechanically. In the next few years Horseley,[8] Gowers,[6] and MacWilliam [13] did similar work, using either levers or tambours connected with the moving foot. All of them report the rate of clonus to be between seven and ten per second, except MacWilliam, who records one case with a rate of 14. Examination of his records, however, shows that the waves are in pairs, and he himself states that this fast rate was recorded with the tambour attached directly to the contracting muscle, whereas the foot was vibrating simultaneously at a rate of seven. This 14 rate, therefore, is evidently an artefact due to the mechanical arrangement of the tambour.

In the years 1904-1907, four other investigators repeated and enlarged upon this earlier work. Their interest hinged largely on the making of a differential diagnosis between "hysterical" and "true" clonus. In their cases of true clonus the rate averaged between five and seven per second. Claude and Rose [2] found that six per second was the usual rate. Axenfeld [1] called it six or seven and found that Jendrassik reinforcement increased the rate. Levi [12] worked on 15 different individuals and found the usual rate to be six or seven, with one case as low as five per second. He states that fatigue increased the rate. His studies on clonus in normal and in hysterical individuals showed that they gave a much more irregular curve than that registered by the organic cases. Eshner [5] also found the rate in organic cases to vary between

5.8 and 8.0 per second, and showed that reinforcement increased the rate.

In the last few years three workers have applied the string galvanometer to this study. Wertheim Salomonson [12] examined several cases of organic disease and made simultaneous electromyographic and mechanical records, which show that the electrical discharge comes at the beginning of the muscular contraction. He found the rate of ankle clonus to be about eight per second, and shows a most interesting record of an hysterical clonus in which there is a continuous tetanus-like series of small waves underlying the larger waves that appear with the clonic muscular contraction.

Gregor and Schilder [8] made electromyograms of the muscular contractions in many forms of nervous disease; among others they show records of patellar and ankle clonus. These are at the rate of 7 to 9.5 and some of the individual contractions give several small action-currents. They mention this point as characteristic, thereby differing from Salomonson [13] who says that there is but one action-current for each clonic contraction. In an earlier paper [7] they had stated that there was but one "impulse" for each clonic contraction. All three of these authors speak of the action-currents as synonymous with the "Innervationsimpulse," an interpretation taken from Piper [14] who did the pioneer work in electromyography.

## METHOD

The apparatus used for recording the action-currents of the muscles studied was the string galvanometer designed by Dr. H. B. Williams and manufactured by C. F. Hindle & Co. This is a standard machine such as is used in "heart stations" for electrocardiographic work. The optical system and recording camera were also the stock type made by this company, except that a special gear was introduced to give greater speed to the film; with this addition a speed of from 20 to 27 cm. per second was obtainable. For electromyographic work of this kind any string galvanometer might be used with slight adaptation; descriptions of such modifications are given by Williams,[15] Snyder [17] and Forbes.[4] The string used was the one supplied with the apparatus and consisted of a gilded quartz fiber 3 micra in diameter with a resistance of 5000 ohms.

Electromyography, or the study of the action-currents of the skeletal muscles, has been described from the physiological standpoint by Piper,[14] but a short description of the method as applied to the study of clonus may be inserted here:

In order to record the electrical changes in a contracting muscle a continuous circuit must be established through that muscle and the string of the galvanometer; thus there must be two electrodes on the body surface, one connected with each end of the string. One of these is applied to the skin just over the belly of the muscle to be studied, and the other is placed over some nearby skin area beneath which there is no muscular contraction. For example, in studying ankle clonus, one electrode is placed over the belly of the gastrocnemius and the other in the popliteal space. In patellar clonus one is over the rectus femoris about 20 cm. above the patella in the mid-line, while the other is fastened to the inner side of the leg about 6 cm. away, over a spot where no muscular contraction takes place during patellar clonus. In this way action-currents of the clonus are alone recorded.

In studying ankle clonus the subject lay prone with the knee-joint fully extended. The skin was washed with soap and water, dried with ether, and the electrodes were then applied to the points designated above. These electrodes were of the non-polarizable type described by Piper [14] and by Forbes.[4] They consist, briefly, of funnels filed off at the small end so as to admit a rubber stopper; a piece of cat's bladder is stretched over the larger end, and a zinc rod is thrust through the rubber stopper into the cell which is filled with a saturated solution of zinc sulphate. The leads from the galvanometer string are attached to these zinc rods and the solution, permeating the animal membrane, makes the necessary electrical connection with the body of the patient.*

With the patient in position and the skin prepared, the electrodes are firmly fastened to the appropriate spots with narrow roller bandages. The galvanometer is then set with the string at such a tension that 1 millivolt causes a deflection of 1 cm. on the record. The connections are made with the patient; the resistance of the patient is measured and compensated, and the camera and lights are arranged for the making of the record. Then an assistant sets up ankle clonus by pressing sharply on the ball of the foot. In the case of patellar clonus the procedure is the same except that the patient lies supine and pressure is exerted on the patella to set up contractions in the rectus femoris.

When stimulation was kept up over a long period of time, as in the fatigue studies, it was found that the assistant became tired before the clonus, so it was necessary for the galvanometer operator to change places with him every five or ten minutes. This gave a short hiatus in the continuity of the clonus, but not of long enough duration to admit of much recovery from fatigue.

In some experiments the effect of a light pressure on the ball of the foot was compared with that of strong pressure. No accurate quantitative measurement of these variations in stimulation was attempted because only the grosser variations seemed to cause any corresponding changes in the periodicity, rate, and size of the action-current.

In relation to the leaking out of the zinc sulphate solution from the electrodes an interesting artefact was noticed which has been considered as possibly a physiological manifestation by Wertheim Salomonson.[12] In his records of clonus, he noticed that sometimes there was a slow wave following the quick action-currents. In the present experiments it was found that such slow curves always appeared when the solution leaked out of the electrode, allowing the membrane to

* The leaking out of the zinc sulphate solution was often troublesome. An easy way to overcome this was devised by placing a funnel of slightly larger size tightly over the completed electrode and filling in the space between the two funnels with celloidin, thus effectively sealing up the loose connection between the cat's bladder and the inner funnel.

retract slightly from the skin and thus to cause a change of contact with each movement of the underlying muscle. Accurately applied electrodes would give no slow waves at the beginning of an experiment, but during the next 15 minutes there would be a gradual appearance of such waves coincident with the leakage from the electrode (Fig. 1).

FIG. 1.

In this figure the upper tracing shows an electromyogram taken with the electrodes in firm contact with the skin (Table IX, Film 3). The lower tracing was made 11 minutes later with electrodes unchanged except for leakage of zinc sulphate (Table IX, Film 9).

## OBSERVATIONS

By the method described above, five patients were intensively studied; two of these had patellar clonus alone, two had ankle clonus alone, and one had both patellar and ankle clonus. The results of these observations are arranged below in nine tables.

The first patient, H. A., was a boy of 16 with a right-hemiplegia for 13 years. The initial lesion was probably an embolus. During the last two years he had been having epileptiform convulsions. The right leg showed both ankle and patellar clonus and both the right arm and right leg showed extensor weakness. Babinski's sign was present on the right.

The next patient, J. M., was a boy aged eight, admitted March, 1918, for broncho-pneumonia. In June, 1914, he was admitted in a delirium; he was found to have typhoid fever and bilateral ankle clonus without Babinski's sign. In July of that year he had a period of psychotic behavior. In 1916 he had rheumatic fever, and in November, 1917, he came back with choreiform twitchings that were thought to be habit spasms. The clonus was more marked in 1918 than at any time previously observed.

The third patient, R. P., male, aged 40, had phthysis 11 years ago, and eight years ago headaches with loss of sphincter control and weakness of the right leg. For the last five years he had had unconscious attacks. A diagnosis of cerebrospinal syphilis was made on the laboratory findings. There was slight weakness of the right leg with ankle clonus and a positive Babinski.

E. L. was a boy of 14, whose illness began six months ago with drowsiness, unsteady gait, and incontinence. From the physical examination a diagnosis of cerebellar tumor was made and an exploratory operation was performed. The tumor was not located, but great intracranial pressure was relieved. The patellar clonus which was present in the left leg before operation disappeared thereafter.

M. S. was a woman of 40, who had had pain in the arms and legs for five years, with staggering, ataxia, and slight bilateral spasticity for one year. There was hypertension and the fundi showed extensive arteriosclerosis. Both legs showed patellar clonus, slight ankle clonus, and Babinski.

In arranging these tables, the time at which each record was made is placed in the first column. In the second column is the number of the film. The third column is headed "Periodicity." This signifies the length of time elapsing between the beginning of one contraction and the beginning of the next in a clonus series. It is taken for granted that the appearance of the first wave in the electromyogram of a contraction bears a constant relation to the beginning of the mechanical contraction of the muscle. Simultaneou mechanical and electrical records made by Salomonson[1] show the reliability of this criterion. In recording the periods of the clonic contractions, each period was measured with dividers and read off against the time as registered in fiftieths of a second by the tuning-fork. If the same length of period repeated itself this was indicated by writing the number of times of the repetition above and to the right of the number. For example in Table I,

TABLE I.—ANKLE CLONUS
(H. A., March 8, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.15 | 1 | .18, .15$^{5}$, .14, .15$^{2}$ | 6.6 | 2. | 110 | 2 | |
| 3.16 | 2 | .16$^{5}$, .17, .16$^{4}$ ... | 6.2 | 1.5 | 110 | 3 | |
| 3.18 | 3 | .16$^{4}$..... | 6.2 | 3 | 110 | 2 | |
| 3.18 | 4 | .14$^{8}$..... | 7.1 | 2.5 | 120 | 3 | |
| 3.20 | 5 | .15$^{23}$..... | 6.6 | 2. | 120 | 3 | |
| 3.21 | 6 | .14$^{4}$, .15$^{5}$ ..... | 6.8 | 2. | 110 | 3 | |

TABLE II.—ANKLE CLONUS
(H. A., April 27, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks<br>Continued clonus from 3.16 to 3.31 |
|---|---|---|---|---|---|---|---|
| 3.16 | 1 | .16$^{13}$..... | 6.2 | 1.5 | 130 | 4 | Light steady stimulus. |
| 3.17 | 2 | .18, .17$^{11}$, .16$^{2}$, .17, .15. | 5.9 | 2.5 | 130 | 5 | Same stimulus. |
| 3.22 | 3 | .17, .18$^{4}$, .14$^{2}$, .16. | 6.0 | 1.0 | 145 | 5 | Light steady stimulus. |
| 3.22 | 3 | .23, .18$^{2}$, .16$^{4}$, .15$^{7}$. | 6.4 | 2.5 | 130 | 6 | Sudden increase in stimulus during record. |
| 3.25 | 4 | .17$^{5}$..... | 5.8 | 1.0 | 160 | 6 | Light steady stimulus. |
| 3.25 | 4 | .20, .19, .17$^{2}$, .16, .15$^{3}$, .14, .15, .16, .18, .17. | 6.1 | 3.0 | 140 | 6 | Sudden increase in stimulus during record. |
| 3.27 | 5 | .18$^{2}$, .17$^{2}$, .18... | 5.6 | 0.7 | 160 | 7 | Light steady stimulus. |
| 3.28 | 6 | .15$^{4}$, .14, .15$^{2}$, .14, .15$^{2}$..... | 6.7 | 2.5 | 160 | 5 | Strong stimulus. |
| 3.28 | 7 | .16, .15$^{2}$, .16$^{6}$... | 6.3 | 2.0 | 150 | 4 | Continued strong stimulus. |
| 3.31 | 8 | .17, .16, .14$^{2}$, .15$^{4}$ | 6.6 | 2.5 | 135 | 5 | Continued strong stimulus. |

TABLE III.—ANKLE CLONUS
(J. M., March 20, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 2.35 | 1 | .16, .14, .12[11], .13[2], .13, .14[2], .13[3], .15[2], .12[2], .15. | 7.8 | 3. | 80 | 2 | |
| 2.45 | 2 | .15, .14[3], .15, .14[23]. | 7.1 | 1. | 100 | 2 | |
| 2.47 | 3 | .14, .13, .14, .12, .14[2], .12, .14, .12, .12[2], .13, .14. | 7.6 | 2. | 150 | 3.5 | A few waves between contractions. |
| 2.47 | 4 | .13[3], .12[2], .14, .12[4], .14, .12. | 7.6 | 1.5 | 150 | 3.5 | |

TABLE IV.—ANKLE CLONUS
(J. M., April 13, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.25 | 1 | .26, .16[2], .16[2] ... | 6. | 3.5 | 150 | 4 | Irregular, discontinuous clonus. |
| 3.27 | 2 | .13[2], .14, .13[2], .14, .13, .14, .13[5]. | 7.6 | 5. | 125 | 3 | Clonus regular and continuous. |
| 3.28 | 3 | .13[10]..... | 7.6 | 6. | 125 | 3 | Clonus regular and continuous. |
| 3.29 | 4 | .14, .13[7]..... | 7.6 | 6. | 125 | 3 | Clonus regular and continuous. |
| 3.30 | 5 | .13[10]..... | 7.6 | 4.5 | 125 | 4 | Clonus regular and continuous. |
| 3.31 | 6 | .13[2], .14, .13[2], .12, .14, .13[5]. | 7.6 | 4. | 110 | 2 | Clonus regular and continuous. |
| 3.32 | 7 | .13[5]..... | 7.6 | 5. | 110 | 3 | Clonus regular and continuous. |
| 3.35 | 8 | .13[9]..... | 7.6 | 3.5 | 110 | 3 | Clonus regular and continuous. |
| 3.36 | 9 | .14[10]..... .... | 7.1 | 3.5 | 110 | 3 | Clonus regular and continuous. |
| 3.38 | 10 | .13, .15, .13[3].... | 7.5 | 4. | 110 | 3 | Clonus regular and continuous. |
| 3.39 | 11 | .13[7]..... | 7.6 | 3.5 | 135 | 4 | Clonus regular and continuous. |
| 3.41 | 12 | .15, .14, .13.... | 7.1 | 3.5 | 135 | 4 | Clonus regular and continuous. |
| 3.44 | 13 | .13, .14[2], .15, .13, .15, .14, .15[2], .14.[5] | 7.1 | 4. | 135 | 4 | Clonus regular and continuous. |
| 3.46 | 14 | .13[3], .14, .13[2], .14 | 7.6 | 3. | 135 | 3 | Clonus regular and continuous. |
| 3.48 | 15 | .14[2], .13[4]..... | 7.5 | 3. | 135 | 3 | Clonus regular and continuous. |
| 3.50 | 16 | .13[4]..... | 7.6 | 3.5 | 135 | 4 | Less continuous, needs a forcible flexion every min. or two to keep it going. |
| 3.54 | 17 | .13[9]..... | 7.6 | 4. | 100 | 3 | Patient begins to complain of fatigue. |
| 3.55 | 18 | .13[5], .12[2]..... | 7.6 | 4. | 110 | 4 | |
| 3.57 | 19 | .12[3], .13[3], .13, .12, .13, .12[3], .13. | 7.9 | 4.5 | 135 | 4 | Stronger stimulus. |

TABLE V.—ANKLE CLONUS
(R. P., April 15, 1918)

| Time P. M. | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks<br>Clonus kept up from 2.35 to 2.59 |
|---|---|---|---|---|---|---|---|
| 2.35 | 1 | .21, .18, .16[4], .15[2], .14[3], .16[2], .14[3], .15[4]. | 6.6 | 3.5 | 110 | 5 | |
| 2.36 | 2 | .20, .18, .16[4], .15[2]. | 6.4 | 3.5 | 110 | 5 | Fresh stimulus. |
| 2.39 | 3 | .20[2], .16[7], .14, .15[3], .16, .17[2], .15[100]. | 6.5 | 3. | 120 | 6 | Fresh stimulus. |
| 2.42 | 4 | .22, .20, .18[3], .16[4], 15[51]. | 6.5 | 3. | 125 | 5 | Fresh stimulus. |
| 2.45 | 5 | .18[10]..... | 5.5 | 1.5 | 100 | 5 | Sample out of a 3 min. steady clonus from one stimulus. |
| 2.50 | 6 | .16[9]..... | 6.2 | .2 | 150 | 4 | Fresh stimulus at 2.48. |
| 2.55 | 7 | .16, .17[6]..... | 5.9 | .2 | 135 | 4 | Sample out of same series. |
| 2.56 | 8 | .17[11]..... | 5.9 | 1.5 | 120 | 3 | Sample out of same series. |
| 2.57 | 9 | .17[4]..... | 5.8 | 2. | 100 | 3 | Sample out of same series. |
| 2.58 | 10 | .18[4]..... | 5.5 | 1.3 | 150 | 4 | Sample out of same series. |
| 2.58 | 11 | .18, .19[2]..... | 5.3 | 1. | 165 | 5 | Sample out of same series. |
| 2.58 | 12 | .19[4]..... | 5.2 | 0.7 | 150 | 4 | Sample out of same series. |
| 2.58 | 13 | .19..... | 5.2 | 0.5 | 150 | 4 | Sample out of same series. |
| 2.59 | 14 | .16, .15[7], .16.... | 6.5 | 3. | 135 | 4 | Strong fresh stimulus. |

N. B. At 2.48 a steady pressure on the ball of the foot was begun and continued without appreciable change until the clonus spontaneously faded away at 2.58½. Then a new strong stretch was given to the muscle, starting up a new clonus at 2.59.

No. 5, the periodicity was .15 of a second for 31 consecutive contractions, this is then written .15[31].

In the next column the records of periodicity are averaged and interpolated into the rate per second of the clonus as a whole. For example, a periodicity of .15 equals a rate of 6.6 per second.

The fifth column gives measurements of the amplitude of the waves recorded on the moving film. These represent the

TABLE VI.—PATELLAR CLONUS
(H. A., March 8, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.35 | 1 | Average .16... | 6.2 | 1.5 | 150 | 2. | Two to three contractions only. |
| 3.37 | 2 | Average .16... | 6.2 | 1.5 | 140 | 2. | Two to three contractions only. |
| 3.39 | 3 | Average .16... | 6.2 | 2. | 120 | 2.5 | Two to three contractions only. |
| 3.41 | 4 | Average .155.. | 6.4 | 2. | 110 | 2. | Two to three contractions only. |

TABLE VII.—PATELLAR CLONUS
(E. L., March 16, 1918. Cerebellar Tumor)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 4.00 | 1 | .20, .20, .16.... | 5.2[1] | 3. | 50 | 1 | |
| 4.02 | 2 | .17, .15[7]..... | 6.6 | 1. | 75 | 2 | |
| 4.02 | 3 | .17, .15[8]..... | 6.4 | 1. | 85 | 3 | |
| 4.05 | 4 | .20 ..... | | 3. | 45 | 1 | |
| 4.06 | 5 | .19. .17[2]..... | 5.7 | 2. | 100 | 2 | |
| 4.08 | 6 | .18, .15[5]..... | 6.0 | 1. | 100 | 3 | |

TABLE VIII.—PATELLAR CLONUS
(M. S., March 29, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.30 | 1 | .16, .14[2], .13[3]... | 7.1 | 1.5 | 75 | 3 | |
| 3.31 | 2 | .14[2]..... | 7.1 | 3. | 60 | 2 | Followed by tetanus for one sec., then stimulus given and followed by tetanus. |
| 3.31 | 3 | .15, .14, .13[3], .12[2]. | 7.6 | 4. | 60 | 3 | |
| 2.32 | 4 | .17, .14, 12[7]..... | 8.1 | 4. | 60 | 2 | After rest of one min. new stimulus, followed by tetanus. |
| 3.33 | 5 | .13[15]..... | 7.6 | 2. | 75 | 2 | Clonus more easily elicited, end of a series recorded. |
| 3.40 | 6 | .13[6], .12[6]..... | 8. | 3. | 75 | 2 | |
| 3.41 | 7 | .13[4], .12, .10.... | 8.2 | 3. | 60 | 2 | Followed by tetanus at rate of 75. |
| 3.42 | 8 | .12[2], .10, .09.... | 8.5 | 4. | 55 | 2 | Running into irregular tetanus. |
| 3.42 | 9 | .17, .15, .13, .14, .12[3]. | 7.7 | 3. | 60 | 3 | |

magnified excursions of the galvanometer string, which in turn were caused by the action currents in the contracting muscle. Their quantitative value lies only in the fact that the tension of the string is so arranged that one millivolt causes a deflection of 1. cm., but this is again affected by the resistance of the patient in circuit, so the figures are only valuable for comparison in a series of observations in which the electrodes are left undisturbed. This is the case in each separate table.

In the sixth column is an average estimate of the rate per second of the action-current waves which go to make up the electromyogram of a single clonic contraction. Those small waves which are not considered large enough to represent an action-current are not counted. A factor of uncertainty, therefore, enters into the estimation of these rates and they must be considered as only approximate. In the next column the number of waves which go to make up the myogram of a single contraction are averaged and recorded. Here again it is difficult to decide whether a small excursion of the string is worth counting as a true wave.

TABLE IX.—PATELLAR CLONUS
(M. A., April 2, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.40 | 1 | .16[2], .13..... | 6.6 | 3. | 70 | 2 | 3 twitches followed by tetanus at rate of 70. |
| 3.40 | 2 | .16, .14, .12[2].... | 7.5 | 2. | 70 | 3 | Slight tetanus after 4 twitches. |
| 3.46 | 3 | .17, .16, .14[2], .13, .12[2]. | 7.6 | 2. | 70 | 2 | Amplitude in mm., 2-1, 5-2-1, 8-3-1-1, 5-1-2-1, 8-1, 5-1-1. |
| 3.47 | 4 | .16[2], .14[2], .13, .14, .13. | 7.1 | 3. | 60 | 2 | Followed by tetanus for 1.4 sec. at rate of 50 per sec. |
| 3.48 | 5 | .16[2], .14[2], .13,. 12. | 7.1 | 3. | 50 | 2 | Followed by tetanus for 1.3 sec. at rate of 60 per sec. |
| 3.55 | 6 | .14[65] ..... | 7.1 | 1.5 | 60 | 2 | Continuous clonus started at 3.53. |
| 3.55 | 7 | .14[15] ..... | 7.1 | 1. | 50 | 1 | Same steady clonus. |
| 3.57 | 8 | .16, .14[5], .13[7]... | 7.3 | 2. | 55 | 2 | New stimulus, and new clonus followed by 1.4 sec. of tetanus at rate of 50. |
| 3.57 | 9 | .14, .13[3], .14[5], .13[2]. | 7.4 | 2. | 60 | 2 | New stimulus, followed by irregular tetanus for 0.2 sec. |

## DISCUSSION

An examination of the above tables brings out several characteristics of clonic contractions. In the first place it will be noticed that the first few periods are longer than the succeeding ones and that it takes some time for the clonus to fall into a steady rhythm (Fig. 5). For example in Table V, Film 4, the first period is .22 seconds and the second is .20, followed by three periods of .18 and four of .16 before the clonus falls into its regular periodicity of .15; this is also shown in the third film of this table, where after a preliminary unsettled series, the contractions finally repeat themselves 160 times at .15 seconds. This seems to be as characteristic of patellar clonus as it is of ankle clonus (see Tables VIII and IX). It also appears that in any series of records the ones toward the end of the experiment are more regular than those at the beginning (see Table IV).

The effect of repeated clonus and of long continued clonus was also studied in relation to fatigue. Other investigators, notably Levi,[13] have stated that fatigue causes an increase in the rate of the clonus. In the present studies such was not found to be the case; in fact the phenomenon seems to be remarkably constant after the steady rate has once been reached. For example in Table IV it is seen that the rate of clonus is six per second at 25 minutes past three, reaching its steady rhythm of 7.6 per second two minutes later. After 21 minutes of continuous and steady clonus the rate is found to be slower, if anything, and at three fifty when the patient complains of fatigue the rate is still 7.6. At three fifty-seven the clonus has been continuous for half an hour and the rate is 7.9, but this is probably due not to fatigue, but to the factor next to be

discussed, namely variation in the strength of stimulus. Patellar clonus seems to be equally unaffected by fatigue: Table IX shows a rate of 7.5, in Film 2, and at the end of 17 minutes of constant clonus the rate is 7.4 contractions per second. In Table V, Films 7 to 13 show a clonus kept up for eight minutes with only one initial flexion of the ankle as a stimulus; the rate is slower at the end than at the beginning. The patient had altogether 24 minutes of clonus and began with a rate of 6.6 and ended with 6.5 per second. Thus it seems that fatigue in itself does not cause an increase in the rate of clonic contraction.

Variation of the strength of stimulus used to excite the clonus does, however, seem to affect the rate. This is well shown in Table V where the long continued clonus drops from a rate of 6.2 per second to 5.2 and then suddenly jumps to 6.5 when a strong fresh stimulus is given (Films 6 to 14). The explanation of this is as follows: at the beginning the assistant who was holding the patient's foot held the gastrocnemius strongly and steadily stretched; after two or three minutes his grip became fatigued and at the end of five minutes he admitted he was feeling tired, so there was without doubt a gradual diminution in the stimulus, corresponding to the fall in rate. When the new forcible flexion is given to the ankle at two fifty-nine the rate immediately increases from 5.2 to 6.5 per second. In Table II there are recorded experiments especially made to demonstrate this point: at first a light steady pressure was kept on the ball of the foot for six minutes, and the rate of the clonus varied between 6.2 and 5.9 per second. Then a sudden increase in stimulus was given and the rate quickened to 6.4. With the relaxation of this pressure it dropped again to 5.6 and when a continued strong stimulus was given the rate stayed for three minutes between 6.3 and 6.7. It is interesting to note in Table II, Films 3 and 4, that a sudden increase, although it quickens the average rate, first causes a few slow periods like the slow onset of an entirely new clonus.

The amplitude of the waves is the only factor that seems to keep pace with the strength of stimulus and the rate of clonus. With a strong stimulus and quick rate the electrical discharge from the muscle causes higher waves to be registered on the electromyogram than when the stimulus is weak and the rate slower. This shows well in Table II and is conspicuous in Table V. Where there is a new strong stimulus applied to the muscle the waves average from 3 to 3.5 mm. in height, but in the long continued clonus (in Films 6 to 13, Table V) a gradual decrease is shown, the last waves being only 0.5 mm. in height, increasing suddenly again to 3 with the new stimulus. Table II shows records of observations where the increased stimulus was applied while the record was being taken. In Film 3 a light steady pressure was being kept up which gave waves with an average height of 0.1 mm. The stimulus was then suddenly increased and the size of the waves immediately became 2.5 mm. In Film 4 this same thing is repeated with an increase of 300 per cent in the amplitude of the waves. Thus with an increased stimulus and quickened rate the electrical discharge seems to increase.

The 6th and 7th columns in the table show little of importance and too few cases were studied to make any general conclusions, but it may be worth noting that in patellar clonus (Tables VI, VII, VIII, IX) the individual contractions are usually made up of only two waves the rate of which average 80 per second, whereas ankle clonus showed about four waves to each contraction with an average rate of 125 per second. This suggests that patellar clonus is a simpler mechanism than ankle clonus, approximating more nearly a series of tendon reflexes. Salomonson [15] says that in true clonus there is but one action-current for each contraction, and that if two or more are found they are to be considered artefacts due to an "interference phenomenon." He believes that such interference arises when the electrodes are wrongly placed on the muscle. The presumption is that the electrodes are so placed that a single action-current is recorded more than once.[15] That groups of action-currents from a single contraction of a clonus series are not due to such an artefact is proved by recording a tendon reflex which shows a single diphasic wave (Fig. 6) and then, with the electrodes unaltered, eliciting a clonus which shows several action-currents to each contraction (Fig. 7).

A correlation of the height of the patient with his rate of clonus indicates that small size and high rate of the clonus go together. H. A. and M. S. were the smallest patients, and their average rate was 7.6, the others averaging 6.5 per second. This falls in line with the observations of Alexander James [16] who states that "the rapidity of ankle clonus is in inverse ratio to the height of the individual."

Most observers who have written on the subject of clonus have tried to differentiate sharply "true clonus" from "voluntary clonus" or "hysterical clonus." [8 12 13] Since this paper deals with only five cases, all of which are obviously "organic" it might seem irrelevant to take up the discussion of this differentiation, but in one case of patellar clonus (Table VIII) a constant tendency was noticed for the clonus to go over into a tonic cramp-like contraction (Fig. 4). This tonic contraction gives a tetanic series of waves resembling those shown by Salomonson in hysterical clonus and others shown by Gregor and Schilder [8 (Fig. 47)], where a voluntary contraction of the quadriceps muscle turns into a typical patellar clonus. The case described in Table VIII is one of spastic paraplegia with no hint of hysterical complication. The other case in this series which showed a tendency toward tetanic contractions complicating the pure clonus, in the case of J. M. (Tables III and IV). His records not only always showed several waves to each contraction, but also an occasional wave or a short tetanus was found between the clonic contractions. The fact that this is the case of post-typhoidal clonus without Babinski's sign makes one wonder if there is a possible "voluntary" component here, especially as the boy stated that he liked to balance his foot so it would jerk, and enjoyed the interest taken in him by the physicians. Because of such facts as these it seems wiser to make no sharp distinction between the "true clonus" of organic origin, and the "pseudo clonus" of hysteria. In the present state of our knowledge it is more reasonable to think of clonus as a slow, rhythmical neuro-

FIG. 2.

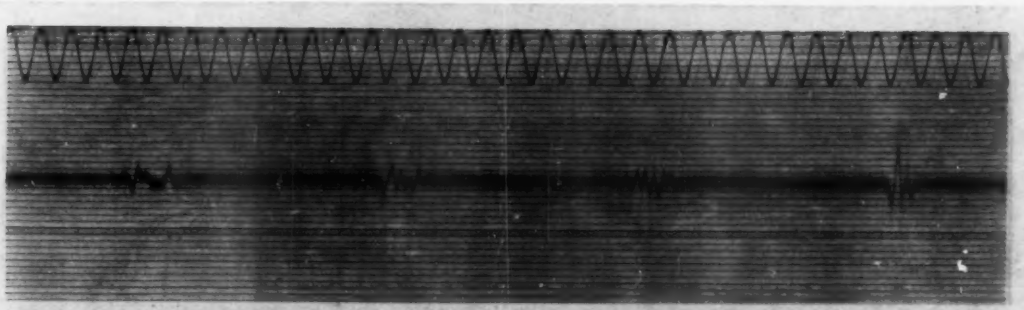


FIG. 3.

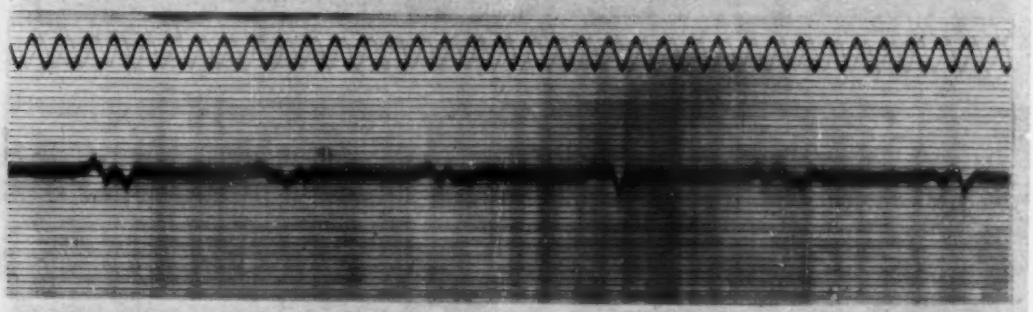
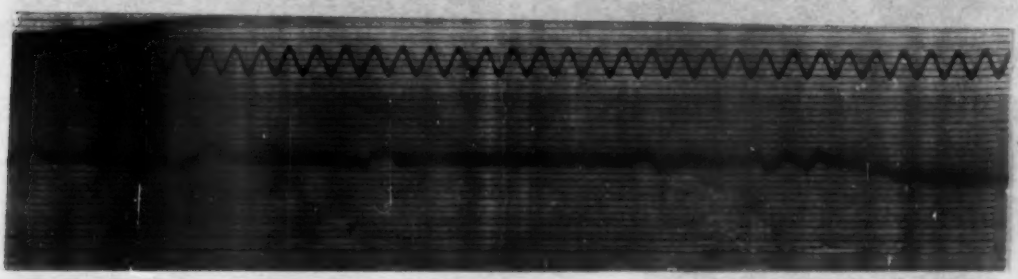


FIG. 4.



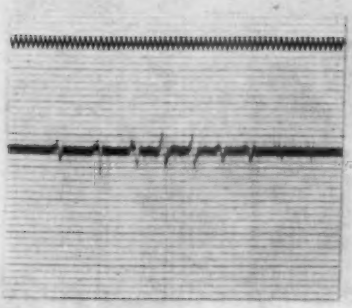


FIG. 5.

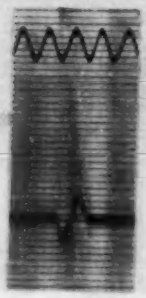


FIG. 6.

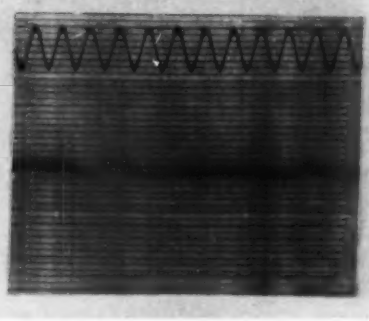


FIG. 7.

muscular phenomenon which may be more or less complicated by the faster rhythms of the psychobiologically determined "voluntary" contraction.

### THEORETICAL

There is probably no distinct line between clonic and sustained muscular contraction. Voluntary contraction is sustained, giving a tetanic electromyogram, but certain individuals can voluntarily induce a clonus. It is notable that such a clonus falls into the usual rate of about 7 per second,[1 2 10] but it is less regular than the pathological clonus studied in this paper, and it can only be elicited by people with hyperactive reflexes or after fatigue of the muscles involved.[2] In this connection it is interesting to remember that clonus is found after wasting diseases such as typhoid fever.[10] Then there is the great group of hysterical clonus which resembles the voluntary type. Only one hysterical case has been studied electromyographically,[5] but this one shows a definite tetanic (voluntary) rhythm underlying the clonus. It should be of great interest therefore to study all clonic contractions electromyographically. In this way a new diagnostic criterion might be found between hysterical and organic cases. The question would be what difference one might find in the clonus in states of normal psychobiological integration and in states of hysterical malintegration, when compared with the organic cases. In purely organic clonus there is no sign of electrical activity in the muscle between contractions. It is interesting that in the case of M. S. where the patellar clonus passes over into a tetanic spasm, the rate and the number of action-currents per contraction increases as the spasm comes on, until the tracing becomes that of a continuous contraction (Fig. 4). Illustrations of the opposite condition are shown by Gregor and Schilder [8] (Figs. 47 and 48) where attempts at voluntary contraction of a paretic muscle give electromyograms showing transition from tetanus to clonus.

Most writers on clonus agree with Langelaan [11] who states that clonus is a reflex symptom, or a series of them; and that the stretching which follows a contraction is a new stimulus to the proprioceptors and calls forth another reflex twitch; thus the symptom propagates itself until fatigue or inhibition puts an end to it. If this were the true explanation of clonus we would expect a much shorter periodicity than that which is observed; Snyder [11] found that the reflex time of the knee jerk was about 0.011 seconds. If then clonus was purely a self-propagated proprioceptive reflex we would expect it to have a much higher rate, for in eliciting clonus we keep the muscles stretched, thus stimulating their proprioceptors, which can reflexly cause a contraction in 0.011 of a second; the muscle then relaxes only to find the stretching stimulus still there to set up another contraction. The fact that the average periodicity is 0.15 seconds when the reflex time is only 0.011 must be explained.

There seem to be three theoretical possibilities. First, it may be that the relaxation time of the muscle takes up 0.1 of a second or more. Secondly, a summation of stimuli through the proprioceptors may be necessary to cause the next contraction. And lastly central inhibition may play a rôle. The first two possibilities should be studied experimentally. For the last there is some clinical evidence already; evidence for the existence of some energy constantly tending to excite muscular contraction, but normally held in check by inhibition. Removal of this inhibition by decerebration, by central lesion, or positive motor effort, causes more or less permanent muscular contraction. There seem to be all degrees, from slight spasticity to permanent contracture, but the interesting point is that whatever the cause of heightened muscular tone may be, the rate of the clonus (or of the tremor in such diseases as paralysis agitans) falls always into approximately the same rhythm.

Piper, Salomonson, Gregor and Schilder speak of "Innervationsimpulse" when referring to action-currents in muscles, taking for granted that each action-current represents a single nerve impulse. This theory is not supported by the more recent investigations of Forbes and Rappleye [5] who have shown that warming and cooling the muscle changes the rate of its action-currents. They conclude (p. 254) that "the rhythm observed in muscle response is not the rhythm of motor nerve impulses, but is dependent, as Buchanan maintains, on the condition of the muscle." Action-currents therefore, must be looked upon as electrical concomitants of neuromuscular activity, their rate and character being controlled not only by the rate of the nerve impulse, but also by the physiological state of the muscle itself.

In closing I wish to express my appreciation to Messrs. L. S. Chapman and P. R. Holtz for their help in making the galvanometric records. I also wish to thank Dr. Meyer for his interest in the work, and the other physicians of the hospital who gave me the opportunity to study their cases.

### CONCLUSIONS

(1) Electromyography is a more accurate and more easily applied method for the study of muscular phenomena than those formerly applied to clinical observation.

(2) Clonus gives a characteristic electromyogram.

(3) Fatigue does not affect the rate of clonus.

(4) Increased stimulus increases the rate of clonus and the size of the electromyographic waves, but does not change the rate of the action-currents.

(5) The number of action-currents per contraction varies with the type of the clonus.

### BIBLIOGRAPHY

1. Axenfeld: Arch. di Fisiol., 1907, IV, 160.
2. Claude and Rose: Rev. Neurol., 1906, XLV, 829.
3. Eshner: J. Am. M. A., 1904, XLII, 1202.
4. Forbes and Gregg: Am. J. of Physiol., 1915, XXXVII, 118.
5. Forbes and Rappleye: Am. J. of Physiol., 1917, XLII, 228.
6. Gowers: Man. Dis. of the N. S., 1893, 2d edition, II, 17.
7. Gregor and Schilder: Münch. Med. Woch., 1912, LIX, 2851.
8. Gregor and Schilder: Ztschr. f. d. g. Neurol. u. Psych., 1913, XIV, 359.
9. Horsley: Brit. M. J., 1885, I, 112.
10. James: Edin. M. J., 1880, XXVI, 135.

11. Langelaan: Neurol. Centralbl., 1904, XXXIII, 1140.
12. Levi: Arb. a. d. Neurol. Instit. Wien. Univ., 1917, II, 28.
13. MacWilliam: Brit. M. J., 1901, II, 1595.
14. Piper: Electrophysiologie menschlicher Muskeln, Berlin, 1912.
15. Salomonson: Folia Neurobiol., 1910, IV, 1.
16. Snyder: Am. J. of Physiol., 1913, XXXII, 329.
17. Snyder: Am. J. of Physiol., 1910, XXVI, 474.
18. Tileston: Am. J. Med. Sci., 1913, CXLVI, 1.
19. Williams: Am. J. of Physiol., 1916, XL, 230.

DESCRIPTION OF PLATE

FIG. 2.—Ankle clonus; electromyogram from gastrocnemius muscle. (See Table II, Film 2.)

FIG. 3.—Patellar clonus; from rectus femoris muscle. (See Table VIII, Film 9.)

FIG. 4.—Patellar clonus ending in spasm, electromyogram showing the transition from periodic to tetanic waves. (See Table IX, Film 5.)

FIG. 5.—Patellar clonus, low speed film, showing that the periods are longer at the beginning, and quickly shorten to a more constant periodicity, in this case the periods are: .17, .14, .12". (See Table VIII, Film 4.)

FIG. 6.—Patellar reflex, showing single diphasic wave.

FIG. 7.—Patellar clonus, record taken immediately after Fig. 6 without shifting electrodes. Clonus set up by steady pressure on patella. Note that each contraction has several action-currents.

In each case the upper tracing is the shadow of the tuning-fork vibrating at 50 D. V. per second, and the lower is the electromyogram.

# LAVOISIER AND THE HISTORY OF THE PHYSIOLOGY OF RESPIRATION AND METABOLISM. CONTEMPORARY VIEWS OF LIFE PROCESSES

By JOHN C. HEMMETER, M. D., PHIL. D.

Antoine Laurent Lavoisier, the son of a rich merchant, was born August 26, 1743, in Paris. Little can be ascertained concerning the degree of culture and the intellectual status of his parents. Alphonse de Candolle in his "History of Science and of Scientific Men" gives no reference to the genealogy. De Candolle, a member of the Academy of Sciences, Paris, would have been in a position to ascertain the truth on this point. Galton and Wilhelm Ostwald, who endeavored to trace the ancestry of Lavoisier. Prof. Edouard Grimoux (Lavoisier) gives the genealogy of this famous chemist on the paternal side back to 1620 (see Grimoux, pp. 325-331). There is no one in the list of ancestors from whom it could be claimed that Lavoisier received his great genius by hereditary transmission. The studies in the hereditary transmission of genius by Galton, de Candolle, Ostwald, and Raibmayr, find no family basis for their theories in the genealogy of Lavoisier. He was educated at the Collège Mazarin, his studies being directed towards the study of law. He soon developed a preference for natural science. He was instructed in astronomy by La Caille, in chemistry by Rouelle, and in botany by Bernard de Jussieu.

The earliest of Lavoisier's inquiries was an "Analysis of Gypsum," presented to the Academy of Sciences in 1765, and published in the collection of "Mémoires de Divers Savants," 1768. His next work of importance was a paper on "The Practical Illumination of the Streets of Paris," for which a prize had been offered by the Chief of Police, M. de Sartine. This prize was not awarded to Lavoisier, but his suggestions were of such importance that the King directed that a gold medal be bestowed upon the young author at the public sitting of the Academy in April, 1766. Two years later, at the age of 25, he was admitted to the French Academy of Sciences.

He sought and received appointment as "Fermier Général," a position unique in the French Government of that day. The closest approximation to it appears to be a sub-officer in the Department of Agriculture, controlling mainly the revenues (tax on salts, state sales on tobacco, etc.).

In this position he showed himself a skilful administrator. In 1776 Tourgot placed him at the head of the Régie des Salpêtres, where he introduced many improvements into the manufacture of gunpowder. From 1778 to 1785 he gave attention to agriculture and contributed many valuable suggestions to the science of husbandry. In 1787 he was elected to the Provincial Assembly of Orléans. In 1788 he became one of the trustees of the Bank of Discount and in 1789 he was an assistant deputy to the Constituent Assembly. In 1790 he was a member of the Commission on Weights and Measures and developed great interest in the preparation of a new decimal system. In 1791, as one of the commissioners of the Treasury, he published an essay "De la Richesse Nationale de France," in which he presented a plan for the collection of taxes. It was said by the Minister of Public Instruction (who published all of his works from 1864 to 1893) that this essay was a forerunner of a complete treatise on this important subject, and entitles him to a high rank among political economists.

In the "Œuvres de Lavoisier," "*publiées par les Soins de son Excellence, le Ministre de l'Instruction Publique,*" 1864-1893, the incontrovertible evidence of great gift of exposition, power of logic and unparalleled acuteness is manifested. These works embody the principles out of which chemical science was to be renovated. His greatest work is his "Traité Elémentaire de Chimie," 2 vols., 1789, in which the basis of modern chemistry is laid. In 1777 he published in the "Memoirs of the Academy of Sciences" an essay, "Du Principe Constitutif de la Chaleur," which marks the transition of his attention to the application of chemistry to physiology. Some of the more specific experimentations on physiologic chemistry will be explained at a later stage. By this time, the revolutionary movement against Louis XVI and

ANTOINE LAURENT LAVOISIER. BORN AUGUST 26, 1743. EXECUTED DURING THE FRENCH REVOLUTION, MAY 8, 1794.

Marie Antoinette was in full progress. He was collecting all his writings with the ultimate view of remodelling them into a single work, when the course of the revolutionary events brought him to a premature end. Dupin, a member of the Convention, having on May 2, 1794, introduced a formal accusation against all the farmers of the public revenue (Fermier Général) Lavoisier delivered himself up and was imprisoned. On the 6th he was involved in the general sentence of death against the corporation to which he belonged, and two days later he was guillotined. His essays were collected and published by his widow (who afterward married Count Rumford), under the title of "Mémoires de Physique de et Chimie," in two volumes. A complete edition of his works has been published under the supervision of the Minister of Instruction at the expense of the government (4 vols., Paris, 1864-1868).

*Literature.*—Grimaux: "Lavoisier, d'après sa correspondance, ses manuscrits, ses papiers de famille et d'autres documents, inédits (1888)."

Schultze: "Lavoisier der Begründer der Chemie."

Gunning, J. W.: "L'Empirisme et la Science. Esquisse Historique sur Lavoisier. Archive neederland. de sc. exactes, etc. La Haye, 1871, VI, 473-483."

For Portrait, see "Hundred (The) Greatest Men," Vol. 6, London, 1880. Also Purland, T.: Collection II.

Brougham (Henry, Lord Brougham): "Lives of Philosophers," see chapter on Lavoisier.

During the years which followed her husband's death, Mme. Lavoisier was preoccupied with numerous affairs of a personal nature. These finished, she hastened to complete the task undertaken by her husband and arrested by his death.

In 1792 Lavoisier had conceived the idea of publishing his principal data, and of collecting the works of the other scientists who had contributed to the making of modern chemistry a greater science. This work was to be compiled in eight volumes. The first imprint was made at the end of April, 1793. Lavoisier, with the help of Seguin, did the proof-reading during his detention. When he died, the first two volumes were almost entirely printed, as well as a few pages of the fourth. The fourth year (1796), Mme. Lavoisier had a meeting with Seguin in order that these works might appear before the public and asked him to edit a preface, but she required that it should brand the men guilty of Lavoisier's death. Seguin refused. "To denounce those who had him condemned or who let him perish does not strike my fancy and, on the other hand, would diminish the horror that the event has left in all hearts. There are certain things more difficult to tell than to have told by the consciences of those to whom they were presented. Oftentimes they acquire more force from these witnesses. If you do not agree with me, you may have your own views printed; in your own words they would acquire a more convincing tone, proceeding directly from you." (Letter from Seguin dated July 18, 1796.) At the same time, he sent with this letter a sample of a preface which could never have pleased Mme. Lavoisier, for he attributed to himself an equal part with Lavoisier in the project of the publication of the works, saying, for example, "The plan *we* had thought about, the design *we* were meditating," etc.

Mme. Lavoisier gave up the project temporarily but took it up a few years later. She edited an introduction herself, in which she explained the conditions under which Lavoisier had undertaken this work. We publish it in its entirety:

**In 1792, Lavoisier conceived the idea of making a collection of all his works that had been read at the Academy during the 20 preceding years. In a way, it was the making of modern chemical history.**

**To make this history more interesting and more complete, he had proposed to add the works of those who, having adopted his system, had made experiments in his behalf.**

**This collection was to number about eight volumes.**

**Europe knows why they were never completed.**

**Almost all of the first, all of the second, a few pages of the fourth, have been finished.**

**Many scientists have desired to see those published. We hesitated a long time. It is difficult not to feel a certain fear when it comes to publishing the unfinished works of a man who justly enjoys a great reputation. It is when we have lost him that friendship must become impartial and show only what might add to the glory of a cherished and honored name.**

**We would have persisted; and their fragments would never have appeared if they had not contained (page 78 of the second volume) one of Lavoisier's ideas which claims, from the accompanying proofs, that he was the founder of the new chemical theory.**

**Thus it becomes a duty to confirm the views which scientists have expressed in regard to this question.**

**We beg their indulgence for the mistakes that may have been made in some other part of this collection.**

**They will surely grant this request when they learn that most of the proofs were reviewed in the author's last moments, and that, although he did not ignore the fact that his murder was premeditated, M. Lavoisier, calm and courageous, compiling a work which he thought would be useful to science, gave a memorable example of the serenity which intellectual purity and virtue can produce in the most unfortunate hours.**

The two volumes of the "Treatise on Chemistry," published in 1805, were not placed on sale, but given to all of the eminent men of this period. Cuvier thanked Mme. Lavoisier in the following words for her gift of the work to the class in sciences at the Institute:

**Madame, the class requests me to thank you for the work which you have so kindly given them, precious to all as well as to each one. Allow me to offer the testimony of my gratitude. All the friends of science are indebted to you for your heroic determination to publish this collection, and to publish it as it had been originally planned, a sad memorial of your loss as well as theirs. These incomplete volumes, these unfinished utterances, make a profound impression. What truth, it seems, we were about to learn in a book which began with so many truths so beautiful and so new, and yet how we feel the horror of the crime renewed in all its force, a crime which has afflicted humanity perhaps for centuries!**

Historical comments upon scientific researches are subject to manifold errors. The language of science has undergone so many changes in the course of time, that it is often difficult to grasp the real ideas of an author, even though he writes in our own mother tongue. The more distant his views may be from ours, the more readily are we tempted to form erroneous impressions of his meaning. Indefinite announcements often have been considered as discoveries, which were actually and really only made at a later period. Deficiency of exact scien-

tific knowledge occasionally produces erroneous ideas, which may engraft themselves as truths, by repetition; whereas, if such false ideas were not permitted to take hold of us, our thoughts would be led in another, safer and surer, direction.

No one can become independent of the influence which intellectual activity exerts upon seemingly wholly different fields of contemporary knowledge. Sensational discoveries are at once applied to other branches of science, and like newly issued coins, no matter how limited in value, are overestimated, until further investigation reveals their inferiority.

All this is true of our own time, and if this is so, we may conclude that much which is regarded as genuine coin to-day will be cast aside as spurious by those who come after us. We have a right to hope, however, that as methods of investigation improve and the true value of the acquisition of knowledge increases, there will be less need for elimination in the future. It is precisely to this matter of advance in the methods of experimentation that I wish to call your attention.

I will not take you back into remote times, only a period of 123 years, and review the ideas which engaged the minds of men of that time on the remarkable phenomena of nature. The great question of the difference between the organic and the inorganic world has from ages immemorial been uppermost in the mind of the scientist.

The status of the natural sciences about the middle of the 18th century was by no means a low one. Bacon in a most exemplary manner had defined the fundamental principles of inductive research; and eminent investigators, such as Galileo, Kepler and Newton, by observation and experiment, had established the most important fundamental laws of physics. In the science of man, the advances in anatomy by Vesalius were enhanced by the discovery of the circulation of the blood by Wm. Harvey, and placed upon a firm basis by the work of Haller. Chemistry enjoyed special growth about this time and we shall consider this with greater detail since the activity of Lavoisier is most intimately associated with its development.

In my biography of Haller (JOHNS HOPKINS HOSPITAL BULLETIN, Vol. XIX, March, 1908) I referred occasionally to one who stood at the head of science of that epoch—Geo. Ernst Stahl—one of the foremost minds of his time, whose views not only controlled chemistry, but general medicine as well. Stahl's influence rested upon the fact that he understood how to gather together into one general viewpoint the various natural sciences of his time. We may at this day reject as false his so-called "phlogiston" and "anima" theories, but we must not forget that both had a great value, because the sum total of the then existing knowledge was embraced in a unity in Stahl's doctrines which thereby accomplished what we now expect from each single theory.

When Lavoisier began his career, the phlogiston theory was universally recognized and he too was fully in accord with it, for he included the hypothetical heat substance and light substance in his table of chemical elements. (See Wilhelm Ostwald: "Die Forderung des Tages," p. 18.) Looking upon his researches from their beginning, we can trace, step by step, the method by which he at first hesitatingly, then with ever-increasing certainty, began to doubt, and with convincing passion for new truths, began to criticize and finally demonstrate the untenableness of the hypotheses of Stahl.

Lavoisier did not bring about this advance by his own exclusive efforts, but by the adroit use of the discoveries of his contemporaries. He is, however, clearly entitled to the honor of having originally applied the measures adopted at a later time in chemical processes and by which he really is to be looked upon as the founder of modern chemistry. Borutteau in Neuberger and Pagel's "Handbuch der Geschichte d. Medizin" calls him the *"Vater der modernen Chemie."*

It is not my intention to review in general all the work of this great man. His achievements proper have been detailed sufficiently often, and for lack of proper time I must refer you to the excellent statements of Grimaux, Neuberger and Pagel (*l. c.*), Kopp, Ladenburg, E. V. Meyer, Würtz, Lord Brougham, and others. One more point I wish to dwell upon, namely: Lavoisier's demonstration of *the established fact that in chemical processes the amount of matter present is neither increased nor diminished. This fact, first demonstrated by him in a number of experiments, has since become an established law, the law of immutability of the matter present.* This law applies not only to processes pertaining to inorganic, but also to organic substances and for all interchanges between these and the outside world. Clear as this is to us now, many statements appeared in the text-books during that century contradicting these theories. According to Vauquelin, for example, calcium is generated in the body of the chicken, because he thought he had discovered that more of this substance was excreted than had been ingested by this animal.

The prominent position which Lavoisier holds in the history of physiology is due to his series of researches in special physiologic chemistry, overthrowing the then existing *"vitalism"* of Stahl as in his chemic investigations he destroyed the *"phlogiston"* doctrine.

The subject of fire and heat has attracted the attention of naturalists from time immemorial. Stahl (1660-1734) explained these phenomena by affirming that "heat matter" was contained in all combustible bodies and was made to appear when such bodies were burned. He called this heat matter *"phlogiston."* Lavoisier, however, showed that the burning of combustible substances—coal for example—depended upon the oxygen contained in the air, an element recently discovered by Priestley (1774) and almost simultaneously by Scheele (1775); also that animal respiration is a process of combustion by which this O combines with the other bodily constituents of the animal, and that by this union with O the expired air contains $CO_2$ and $H_2O$, as already previously demonstrated by Black. True to his theories, and not satisfied with his general proofs of these processes, he and Seguin made numerous examinations of the expiratory air of man and animals, and thus added largely to the furtherance of our knowledge of the phenomena of life. Since then his experiments have often been repeated by almost identical methods.

When we consider that Lavoisier was the originator of the practical methods, even of elementary organic analyses in use at the present time, and that by the same he demonstrated the composition of the organic substance as made up of C, H, O,

and the occasional presence of N, we can realize that he laid the foundation of physiological chemistry in such completeness that his successors could merely build upon the structure he had created, but for many years could not contribute any material additions. We have, however, not exhausted the subject of the value of Lavoisier's discoveries. A far greater contribution will have to be considered—the explanation of *animal heat.*

Physiologists of all times have endeavored to expound the phenomena that certain members of the animal world, all mammals and birds, during life, possess a temperature far exceeding that of their surrounding conditions, and unchangeable under the most diverse circumstances. Some assumed that this body heat is inborn in the animal, with about as much reason as that of the animists, who held that it was a product of the soul or of the *life-spirit,* to which all the mysterious problems of life were attributed. An exception to this was made by the so-called iatro-mathematicians, who accounted for body heat by the friction of the blood circulating in the vessels, or compared it to heat generated during putrefaction and fermentation, which may have come near enough to truth without leading to further conclusions, as no one understood the cause of heat formation in those conditions. After Lavoisier, however, correctly interpreted the process of combustion and recognized the similarity of the physiologic chemistry of respiration to combustion, he was naturally led to view the heat formation of animals from the same standpoint.

The adherents of the phlogiston theory looked upon fire or heat as a matter, or element, like their other "elements"—earth, water and air. During combustion and the so-called "calcination" of the metals, "phlogiston" and with it heat was liberated from the burning bodies. Later when combustible H gas was discovered by Cavendish in 1781, many claimed that this was phlogiston proper, or air highly charged with it; whilst, on the other hand, O was thought to be "dephlogisticated" air. These views took such a firm hold on the chemists of that time, that even the well-known fact of increase in weight during calcination, which Lavoisier showed to be due to absorption of O, did not convince them to the contrary, but they rather added a new hypothesis, namely, that phlogiston possessed a "negative weight." $CO_2$ was discovered by Black in 1757. N by Rutherford in 1772. O by Priestley, 1774; Scheele, 1775; Lavoisier, 1775; Hirn, 1781.

When, however, Lavoisier had become thoroughly convinced of the untenability of the phlogiston theory, he could not but draw into his investigations the heat that was generated during all processes of combustion. Like other naturalists he still supposed this heat was some form of matter, although unweighable; an imponderable substance, such as magnetism, electricity and the like. Although this conception has been given up, the method of estimating heat, first demonstrated by Laplace and later utilized by Lavoisier to measure the heat produced by animals, still holds good to-day. And since they compared the heat given off with the expired $CO_2$ they believed from their experiments that animal heat was a result of combustion going on in the body.

For the first time a firm foundation was laid for the understanding of the fundamental phenomena of animal life. The conceptions of the times were like this: The animal body is in the main composed of matter consisting of C, H, O and N. These elements may, however, take up a larger amount of O than they originally contain; therefore, they unite with the O transmitted by respiration whereby $CO_2$, $H_2O$ and certain nitrogenous bodies are formed and are expelled. By this combustion, heat is generated. Now since a portion of the body substance is removed by excretion, the animal loses in weight. This loss is replenished by the food substances, which are composed of the same elements as the animal body itself, so that with proper intake it will continue its existence for a longer period of time. Life process, in many respects, may be likened to the burning of a lamp; in fact, the materials fed to the latter are identical in composition with the food-stuffs.

These are the principal features of the theories advanced by Lavoisier as a result of his physiological investigation, of such striking simplicity and so amply verified by experiments, one would think that the physiologists of his time would eagerly seize them in order to emerge from the difficulties of understanding the phenomena of life. This was by no means the case, and by study of the literature of that period, we shall endeavor to ascertain the reasons therefor.

Although the reign of the phlogiston theory fell by the blows given by the chemical discoveries of Lavoisier, and all reputable chemists sided with the antiphlogistic theory (as it was then termed in contradiction), still neither physiologists nor philosophers, and least of all the chemists, in reflecting upon the phenomena of life, could rid themselves of the opinion that these phenomena were of an entirely different order from those of inorganic nature, and, although similar in character in some details, must arise from some special power or cause of their own. Lavoisier's chemical theory of respiration and heat production gave no answer to the difficult question what life really is, and no satisfactory answer to the question, what the hypothetic cause of animal heat was, whether, according to the hypothesis of Paracelsus, it might be called *archeus,* or, according to Stahl, it was the *anima,* the soul or vital force. The thinkers of the time inclined to the same views upon which the alchemists based their theories. Like those who searched for a matter, the *"quinta essentia,"* which should convert all metals into gold, the possessor of which would become wise and immortal, so did these investigators search for a term or formula by which all enigmas would be solved and all secrets disclosed. And since no such formula was discovered, shorter terms, at least, were adopted for the restricted field of phenomena. As to the phenomena of life in particular, some attributed them to vital force itself, others to the *"nisus formativus"* of Blumenbach, and yet others to the "irritability" theory of Haller. The most generally adopted view was that of Stahl, who looked upon the characteristic of life substance as the power of resistance against putrefaction.*

* "Vita nihil aliud est formaliter, quam conservatio corporis in mixtione quadam corruptibili, sed sine omni corruptionis actualis eventu."

In the fortifying and dissemination of these views much was done by a man whose achievements in other fields of scientific labor deserve our fullest recognition, Xavier Bichat. He is the creator of general anatomy, from which our present histology or the finer study of the tissues became developed. As a true adherent to the *vitalistic* school, chiefly upheld by the University of Montpelier, he extensively spread this study in his works and for a long time held unlimited sway. His definition of life, "La vie est l'ensemble des fonctions qui résistent à la mort" ("Life consists in the main of the functions which resist death"), is fundamentally nothing but a transcription of Stahl's theory. Bichat's great influence, especially in his own country, is to be attributed to his elegant and attractive manner of discourse, rather than to the inherent value of his teachings.

According to Bichat, we have to distinguish between two kinds of bodies, animate and inanimate, and two series of phenomena, physical and physiological. The first are produced by physical causes, weight, electricity, etc., the other by physiological, the capacity for extension, contractibility and irritability. The first act according to unchangeable laws, the latter do not. It is therefore impossible to determine the physiological phenomena by the same methods of physical investigation, and he speaks with some contempt of these efforts, clearly alluding to Lavoisier, without, however, mentioning his name.

To this inward impulse for knowledge and the search for an uppermost principle, two especial contemporaneous products of thought came to aid, which again are closely interwoven, *natural philosophy* and *galvanism*. Natural philosophy, in the form given to it by Schelling (system of 1797), had exerted the greatest influence in the development of the natural sciences, especially in Germany. This influence has been much dwelt upon and has met with severe condemnation, which its later excrescences justly deserved. A complete estimate of natural philosophy as conceived by Schelling cannot here be undertaken and only the effects of these theories on the conception of the process of life will be pointed out. Schelling places the highest law of nature upon a trinity: everything springs from two opposite activities, united together by a third—(I) the expanding, (II) the retarding activity and (III) the weight—which are to be looked upon as the equivalent of matter, whereas the latter represents the product of the three activities. Nature as a product of the active substance proper is represented as inorganic, organic and cosmic. The activity of nature is retarded in the first, productivity is continued in the second, whilst in the cosmic the co-existence of the first two is brought about. In *inorganic* nature, the trinity is exhibited as magnetism, electricity and chemism; in the *organic*, as sensibility, irritability and reproduction; in the cosmos, as light, weight (gravitation) and accelerating and retarding force. All organization proceeds from light, which corresponds to world soul, and tends to the production of intelligence. This, however, is attained only in man, the *microcosm*, who also encompasses everything contained in the *macrocosm*, and therefore can produce everything in the form of thought. The laws of nature must therefore be regulated by the laws of consciousness, and the one may be deduced from the other. See Schelling's view of nature in "History of European Thought in the 19th Century," by John Theodore Merz, Vol. III, p. 556, etc.

The broad and sympathetic interpretation of John T. Merz can make even the obscure speculations of Schelling appear interesting to a modern physiologist.

In this system, of which no adequate conception can be made from these preceding sentences, analogies play an important rôle. They must often take the place of proof. The influence of galvanism with its polarities is unmistakable. This very fact induced physiologists of that time to take sides with that system. Galvani's discovery of the wonderful effects of the constant current upon muscles and nerves had made a powerful impression. In galvanism the key was sought and found for the phenomena in nerve and muscle activity and later that of life phenomena. Thus, for example, Prochaska, the Viennese physiologist, in the preface to the renewed edition of his text-book in 1820, states that *"life processes and galvanism rest on the same foundations,"* and boasts that the new edition was worked according to this principle, as is seen from the title on page 47 of the chapter on this subject, *"Life as a matter of fact proceeds from the laws of electrical processes."* The number of treatises on the subject of galvanism which appeared at that time is too great to enumerate. I will mention only one, because it is interesting on account of its author—Alex. v. Humboldt's work in two volumes, on irritability of muscle and nerve fiber.

Looking over the text-books of that time, we find everywhere traces of these influences and I shall refer to one in particular because it is typical. Geo. Friedr. Hildebrandt, professor of physics and chemistry at Erlangen, is best known by his text-book on anatomy, which appeared in 1789-1792, and was revised in 1830-1832 by E. H. Weber, the same who discovered the inhibitory action of the vagus on the heart in 1845. He is also the author of text-books on chemistry and natural sciences, and his work on physiology, first published in 1796, was republished by his son-in-law, Hohnbaum, in its sixth edition, from manuscripts he had left at the time of his death. Hildebrandt was a sober, industrious worker with astonishingly broad knowledge. He constantly emphasized the importance of experience as against construction from general and convincing hypotheses. In spite of this, especially in his later edition, "polar matter" and "*Grundkräfte*" ("fundamental forces") play an important rôle with him. All matter is grounded on the union of the dual expansible and attractive force. These may also become disassociated, in which case the superfluous will act also upon distant bodies. By this are generated magnetism, electricity, chemical processes and the higher stage, life. For this reason both forces act during life; the *expansible* more so, which appears as light in its free state, but in the living body as *life-turgor* (I gather the impression from Hildebrandt's book that he uses the word *turgor*—from turgescere, to swell—as modern physiologists use the word "tonus" or tonicity) by which development and growth are

brought about. The *attractive* force, however, is not missing, for from it we have the chemical and mechanical processes.

All this may impress one as a play of words. The same is felt by the author, for he continues immediately after his exposition, as follows: "However, we must not conclude after these explanations that we have lifted the veil of the secret of life, which covers that of the entire creation. All is hypothesis that our physiologists have to offer as to the problem of life, and what the older physiologists said about the same, although more recent investigations have penetrated deeper into the mysteries of nature than was possible with the former." The "deeper penetration" refers to Schelling's natural philosophy and as pictured in the mind of Hildebrandt. However, on the whole, he was not inclined to be speculative and had he appeared in the middle of the 19th century, he would have been looked upon as a rank "materialist."

According to him, nature yields only matter, coarse and fine; by the latter he means imponderable, and it has been so designated from that time to the present. By admixture only of these, all phenomena are, and even life is, produced, not as Reil thought by mixture and form, because the latter is contained in the former, being generated by it.

Reil plays the same rôle for vitalism in Germany as Bichat does in France. He founded the "Archives for Physiology," the first volume appearing in 1796 and containing an extensive treatise on the life energy—"Lebenskraft." According to Reil, there are two series of phenomena: (1) Matter and (2) conceptions (opinions). The phenomena of the living body, in so far as they are not due to the conceptions or opinions, have their foundation in animal matter, in the mixture of matter (admixture) and form, that is, chemical combination. He holds that "energy" is the relation of these phenomena to the properties of matter by which they are generated; consequently, "vital energy" results from material circumstances, but is not perceptible to the senses owing to the incomplete state of chemistry and lack of knowledge as to the nature of the so-called "imponderables." Therefore, every organ, every tissue, possesses its own vital power due to its chemic composition and form. In his endeavor more closely to confirm these properties, Reil then also resorts to defining life phenomena as "potential galvanic processes."

The unfruitfulness of all these speculations, especially their outgrowths, which natural philosophy of that period carried on, was that no special research for facts was made in single and individual problems or fields of research, but the thinkers aimed to trace everything from the "uppermost principle" by deduction and intuition. This was the reason for naturalists of better mind entirely to turn away from these theories. In justice, however, we must admit that philosophic ideals had a stimulating effect on many branches of our sciences, especially embryology and comparative anatomy. The fundamental phenomena of animal life, however—namely, Lavoisier's discovery of continuous oxidation of its component parts, and the metabolism accompanying it—remained unsolved. Even such an erudite man as Herman Lotze, physician and philosopher, could not arrive at a clear understanding, and as late as 1851, in his "General Physiology," he makes an unsuccessful attempt to explain it teleologically, by the assumption that the body by its continual changes in its component parts is rendered more able to resist outside disturbance. Likewise, the eminent Johannes Müller, who embraced so masterfully the entire physiologic knowledge as it was understood up to his time, could not arrive at a correct conception regarding this fundamental question.

Lotze was one of the first scientifically to attack vitalism, without, however, making much impression. He strove to justify the teleological viewpoint in a philosophical way. It appears possible that this viewpoint can be directly deduced from the premises of the old natural philosophy, but his arguments are defective. As a fact, there undoubtedly is a definite conformity to purpose and to arrangement in organic nature; however, it is not restricted to organic nature, but belongs to nature in its entirety, and to understand the details it is often necessary to ask what purpose or object is fulfilled by this or that part of the whole organization. We must, however, be very careful not to overlook the fact that we are introducing a conception thereby, which can have a meaning only from the standpoint of an individual who acts with a precise and conscious purpose; objects of nature, however, present themselves to our investigation as concrete objects. It is not necessary further to expound to this audience Darwin's theory as to how living things develop conformably to purpose.

Chemists are justified in feeling an inspiring pride in the contributions their historic fellow-workers have made to physiology, for the next impetus to revivifying physiology came from J. Liebig.

After having materially improved upon the elementary organic analysis created by Lavoisier, he applied his vast knowledge of chemistry to the study of conditions of nutrition in animals and plants. What he taught in this field is in part less the result of experimental investigation than it is deductive conclusion from basic chemic principles. Much of this has been found to be erroneous. Nevertheless, he is entitled to the credit of having spurred on the scientific investigation of metabolism and to have again pointed out to physiologists the important significance of Lavoisier's fundamental doctrines.

Before proceeding further, we must go back to the end of the 18th century and consider the life process in plants, especially their nutrition. As early as 1779, Priestley discovered that plants were capable of converting the atmosphere of confined spaces, which had proven fatal to animals, in such a way that the air again became respirable. In the same year Ingen-Housz showed that only the green parts of the plant were capable of doing this, and then only in the light, that they absorb $CO_2$ and exhale O, that contrariwise in the dark all plants, and those not of green color always, take up O and give off $CO_2$ just like animals. In the further course of this research he established his theory of plant nutrition. He showed that the carbon which the plant stores up during its growth could not come from the soil, but from the carbonic acid of the atmosphere, the oxygen of which is liberated whilst the carbon combines with the elements contained in the water

(and in part with N) taken up by the roots. His discoveries were in the main confirmed by Senebier, who, however, erroneously supposed that carbonic acid was absorbed by the roots. Th. de Saussure studied these processes more accurately and demonstrated that larger amounts of $CO_2$ act favorably upon the plant only in strong light (atmospheric air contains but a small quantity of $CO_2$, only 3 to 4 parts in 10,000); that the increase in the weight of the plant is greater than the amount of carbon taken up, because water and salts, the latter in slight quantity only, are absorbed from the soil; that respiration goes alongside with the decomposition of $CO_2$ even in the light; that the plant does not absorb N from the air but from the soil, which was later positively confirmed by Boussingault. If we add to this that Maret in 1834 showed that fungi, which lacking in green coloring matter (chlorophyl) take up O and give off $CO_2$, we shall have summarized what Liebig found already established when he entered the field of investigation of plant nutrition.

In spite of these achievements the practical agriculturists, as well as the theorists, clung to the theory that the so-called "*humus*" was necessary for plant development and that the plant derived its whole sustenance and carbon from it. Liebig had completely set aside this "*humus*" (soil) theory and thereby gave to agriculture a rational principle of fertilizing. For us it is of greater importance firmly to settle the so-called circulation of matter in the organic nature. The plant takes $CO_2$ from the air, N and $H_2O$ from the soil and forms organic bodies from these substances, which with the addition of a small amount of salts make up the greater portion of the plant. Plants serve as a nourishment to animals, directly to herbivora and indirectly to such carnivora as thrive upon herbivora. In these the C is in part again converted into $CO_2$, and H into $H_2O$, whilst another portion of these bodies is excreted in combination with N, in a form which in turn readily passes over into $NH_4$ and as such is again taken up by the plant. The same products result from putrefaction in both animal and vegetable bodies. Therefore, the fundamental law of *conservation of matter* discovered by Lavoisier on a small scale for chemical processes has been shown to take place identically in the larger interchanges of matter transformations throughout the earth.

In spite of the emphasizing of the chemical standpoint in the consideration of life phenomena, Liebig held that these depended upon a special vital power, which, however, did not set aside chemical influences, but directed the same and held them in check. This general view held by all writers of that time may be traced back to the apparent difficulty in understanding how the living body maintains its composition, whereas immediately after death it becomes dissociated by decomposition or putrefaction. In reality this difficulty does not exist, since the living body is constantly being attacked and partially consumed, with this difference, that during life the substances lost are at once replaced.

Whilst up to this time the chemical view was exclusively held with regard to these discoveries, physical views came to the foreground in the middle of the last century, incited by Helmholtz through his epoch-making publication, "On the Conservation of Energy." From this viewpoint du Bois-Reymond in his celebrated introduction to his "Researches on Animal Electricity" explained the untenability of the doctrine of the *vital force* and emphasized particularly that the phenomena of life cannot be differentiated from the inorganic world and that it is the province of science to make plain both series of phenomena upon identical principles in so far as it is scientically possible.

We have seen above in what manner Laplace and Lavoisier attempted to explain that animal heat was slowly produced by slow combustion going on within the body. But their experiments and calculations were not exact enough to settle such an important question. Dulong and Despretz in 1822 sought to determine the matter by new experiments urged on by the prize offered by the Academy of Paris. They arrived at very incomplete results, for according to Dulong only 75 per cent and Despretz 80 per cent of animal heat is generated by combustion. How the balance of 20 and 25 per cent was produced remained a complete mystery. So that it is not to be wondered at, that in the many writings on physiology it was always suggested to that animal heat was something especial, that it was caused by the nervous system, or by vital force, and that, therefore, no constant relationship was necessary between the heat produced and that of the material burned.

Still later, it was shown that neither the experiments of Dulong nor of Despretz nor their methods of calculations offer a binding conclusion and that we have sufficiently concordant estimations in the results of experiments and calculations of caloric values of the nourishment taken, provided we extend the experiments over longer periods and make sure that the animals remain in equilibrium of nitrogen and carbon; *i. e.*, to be in a condition in which an amount of material will be actually oxidized in the organism that is equivalent to the food taken in. This question again depends, as we shall see, upon the law of the "conservation of energy" or as some preferred to call it, "the immutability of stored up energy." By energy we understand the ability to perform work. Daily experience teaches us that the particles of matter attain this ability when they are in motion. A leaden bullet held in the hand is a most innocent object, but when great velocity is imparted to it by the pressure from the gases of the explosion of powder in a gun, it will shatter bone and penetrate steel. Principles of mechanics teach that the energy thus produced can be measured by the work rendered and estimated as one-half of the product of the mass by the square of its velocity. What pertains to the leaden ball holds good for every other substance.

Imagine now two stones of equal weight, one lying on the ground, the other on the roof of a house, and that the latter by some cause is pushed over the edge of the roof. In falling it acquires an increasing rapidity according to Galileo's law. Upon striking the ground it can produce a certain effect or work which the other stone cannot. We see then, that besides *energy of motion*, there is another *energy of position*. The latter differs mainly from the former in that it becomes capable of giving off work when it passes over to energy of motion. It

has been therefore called *latent* or *potential energy* (older term was *elasticity*), whilst the first was termed *living* or *kinetic energy*.

Numerous experiments have demonstrated that energy of position (potential) is true not only for the mass forms of energy, but also for the smallest particles or molecules that go to make up the mass. This is known as chemical combination, but during this process there is a transformation from potential to kinetic energy—comparable to the transformation from the energy of position (potential) of a stone resting on a high place, and the same stone started on a fall downward toward the earth (energy of motion or kinetic energy). By the union of H and O molecules heat is formed, which is assumed to be due to change in the relative positions of H and O atoms. The amount of heat thus generated can be measured by appropriate instruments, just as the heat produced by the impact of a falling object has been measured. The molecules acting in a body seemingly at rest are assumed to be in continual movement, and the energy produced by this inward motion when exerted upon our nerves we designate heat. Now this form of energy may be transformed to the visible motion of masses or reversed, and here again the rule holds that the supply of energy is neither increased nor diminished. Finally, the same rule applies to all known forms of energy, electricity, light, chemical action, etc.

Single portions of this important law of nature were long known to physicists, but the general interpretation was first recognized, though perhaps defined in a vague manner, by the physician, Julius Robert Mayer, of Heilbronn. Helmholtz independently recognized the same law and gave to it a definite mathematic expression, summing up all actual proofs gathered up to that time. These have since then multiplied greatly, but not a single experience is found to contradict this law. We have to conclude then, that there is a supreme law of conservation of energy which substantially supplements the older law of the *immutability of matter*.

To explain the importance of this law for the better understanding of vital phenomena, I must add a word regarding the connection between heat and chemical processes. When in a mixture of H and O the molecules of these gases are set in motion with more or less rapidity, according to the temperature, the median distance between the molecules of these gases remains unchanged. If we apply a flame or electric spark to the mass, a mutual interchange takes place, H and O disappear and we have $H_2O$ instead, in which the H and O unite to form a new combination composed of the same molecules. This is known as a chemical union and may be likened to the process of the falling stone. Like this, the reciprocal position of stone and earth, in the latter the particles of H and O are changed, only that through this change heat is generated, a process that can be measured and estimated by means of the calorimeter. The potential energy (energy of the *position* of older writers) *of the H and O particles* is therefore converted into kinetic energy in the form of molecular motion which we call heat.

Many experiments have shown that in this union of the same quantities of H and O, one and the same amount of energy is involved in the form of heat. One kg. of H oxidized into $H_2O$ produces an amount of heat that will raise 34,000 kg. of water from 0° to 1° C. This is known as the combustion heat of H and we may likewise so designate the combustion heat of C or that generated by any other chemical combination.

Strictly speaking, these figures are not the true expression of combustion heat between H and O. Important reasons lead us to assume that the atoms, the smallest particles in H, are not present in a free state, but united or coupled by twos to form one molecule, the same being true of the atoms and molecules of O. Before union can take place between the atoms of H and O to form molecules of water, the molecules of oxygen and hydrogen must be separated. Since this requires a certain amount of energy, the final result of this combustion is a slightly smaller amount of heat.

The combustion heat is equal to the combination heat minus the so-called molecular latent heat.

This condition must be more fully considered when it concerns complex instead of simple bodies. For instance, the fats are a combination of C, H and O. They are capable of taking on more O and are combustible into $CO_2$ and $H_2O$. Lavoisier, as well as Dulong and Despretz, assumed that as much heat is generated as when equal quantities of free C and H are burned. As a matter of fact, however, the heat produced is smaller, due to the value of the latent heat in the atoms of C, H and O in the fat molecule. Just as heat is liberated by chemical union, we can analyze chemic compounds by heat. Red oxide of mercury is split into Hg and O on heating. The energy used up by this dissociation has always been found to be equal to the heat produced by combining the same elements in the same amounts. The law of conservation or immutabilty of energy applies here throughout.

After these lengthy digressions let us revert to the subject of living objects. Combustion goes on constantly in all animals. Substances containing C and H enter into them and free O is taken in with respiration, whilst both are given off in the form of $CO_2$ and $H_2O$. Heat is thereby generated in all animals, even in the so-called cold-blooded, which are usually not warmer than their environment, because they give up their body heat more readily. Plants also form heat from the O, combining with C and H. In many blossoms—for example, the *Aroides*—in germinating seed and in other similar substances, the formation of heat may be so great as to exceed that which is lost.

Animals not only produce heat, but also produce mechanical work. In a large measure, this is accomplished by the muscles. This act takes place through the energy of chemical combinations. It has been shown that the process of oxidation is actively increased in the working muscles. Working persons excrete more $CO_2$ than those who are inactive. The animal machine which we call muscle is in this respect exactly like a steam engine, a part of the free energy given off appearing in the form of free heat, only that the muscle works under more favorable conditions than the best steam engine. Whereas in the latter only about 10 per cent of chemical energy can be utilized for work, this proportion may under circumstances

reach 25 per cent in the muscle. Count Rumford claimed that a pound of hay given to a horse will yield far greater utilization effect than when the same is used for fuel in a steam engine.* (I have personal doubts as to the feasibility of such a comparative caloric test with the imperfect apparatus available in Rumford's days.)

The mechanical energy generated by combustion in the animal, when not used outwardly for work, is again converted into heat and therefore does not come into consideration in calorimetric investigations, where the animal is confined in a calorimeter. If, however, the experiment is conducted in such a way that some amount of the result is taken up in work, a correspondingly smaller portion of heat is set free, according to the above theory. Hirn, the physicist, has attempted experimentally to prove and estimate this mechanical heat equivalent from the relation between heat and work, but his experiments are not sufficiently exact to claim validity in comparison with the value of the heat equivalents obtained by other methods. In the United States Atwater and Benedict have solved this problem more successfully. For the modern physiology of this subject, see Howell, p. 963, sixth edition.

Animals obtain carbohydrates for nutriment from plants and give off the same in combination with O as $CO_2$. Plants take up this $CO_2$, split up the same and excrete it as O. Whilst energy is set free during the formation of $CO_2$, this must be utilized in the dissociation of the same. This energy is manifestly derived from the sun, since the splitting up of $CO_2$ can take place only in light. There is no doubt that the great heat of the sun represents an enormous storage of energy. A portion of this reaches the earth by radiation and so far as it concerns the green plants it is stored up in the manner described. This not only serves to sustain animal life, but must also serve to liberate heat energy when parts of plants or organic material are burned in stoves. With regard to coal and similar derivatives of plant life used for heating, it is well known that they are the result or effect of the sun's energy, which in part has reached this earth many thousand years ago. (See the "Origin and Evolution of Life" by Henry F. Osborne.)

All life then, animal and vegetable, comes from the sun. But whilst we may be justified in assuming a cycle of events, complete in itself for the organic world, we cannot explain the transformations of energy in the same manner. The energy given off in the form of heat by animals radiates into space in the same manner as the energy from the sun, which has served the purpose of heating the earth's surface. But animal heat thus radiated into space is returned to the sun in but infinitesimal proportions. If, therefore, there are no other special sources besides those of the sun by which we could replenish our supply of energy, and about which we know nothing, the day may presumably come when no more energy will reach the earth. Then all life will cease and the hour hand of eternity will have performed one revolution.

We have arrived at the goal of our travels. Whilst the path was rough and difficult, we have reached a height from which an extensive view over a vast and rich field is presented to us. This path has been largely planned and laid out by Lavoisier, so that but one, it is true the boldest, achievement was needed to reach the climax, and that was by keen research to confirm the law of the conservation of energy.

From this height it is impossible to consider details more accurately. If we step down and carefully examine the field of biological research, we shall recognize the fruits of the labors of so many workers. No opportunity is afforded to mention all. We should find everywhere many actively engaged in gathering in new fruits, sowing seed for future harvests or collecting crops preparatory for future cultivation. We should understand how the aid of chemistry, physics, and the astonishing advances in microscopical technics have cleared up the views of life processes. Above all things our attention would be drawn to a fact of which Lavoisier and his contemporaries had no inkling: the conception of the generation of living beings from elementary organisms or cells. This knowledge first begun by Schwann in 1839 has made tremendous progress. Histology and experimental physiology have continued the examinations of cell structure, as the laboratories of the finer processes of life.

However, let us rejoice in our present possession of truth which will serve as a starting point for new discoveries. Lavoisier's work has helped greatly to put us in possession of these basal truths. Chemists have long ago agreed that Lavoisier is the founder of modern chemistry. You will also admit from the foregoing that physiology also looks upon him as a pathfinder and owes him thanks for some of the most treasured acquisitions. But he also had predecessors who pointed out the way to proceed. As early as 1681, John Mayow recognized that only a portion of the atmospheric air was capable of sustaining respiration and combustion, and that this portion must be contained in saltpetre, for which reason he called it "spiritus," "fixed air." (See also article on Albrecht von Haller, section on respiration, by John C. Hemmeter in Johns Hopkins Hospital Bulletin, March, 1908.)

Going back still further, Leonardo da Vinci, a man of comprehensive and marvellous mind, who combined the genius of an artist with the talent of the scientist, recognized that fire consumed air and that animals could not live in the air which could not support the flame. We must also note that before Lavoisier, Priestley in 1774 produced pure O, and showed that it was absorbed by the blood and that dark blood was rendered bright red by it and that this absorption may also take place through the membranes, an important factor in understanding respiration. Lavoisier has been criticized by Lord Brougham for not being fair in acknowledging the claims of his predecessors. This may be possible, but one thing is certain, it was he who first established the doctrine of respiration and of formation of heat in animals and presented it in such form that all of his successors were enabled to add many single

* Count Rumford's real name was Benjamin Thompson. He was an American, born in Woburn, Mass., in 1753, and later on married Madame Lavoisier, the widow of the great French chemist of whom this article deals. (See Leading American Men of Science, edited by David Starr Jordan.)

details, it is true, but were not able to change the main fundamental principles.

*Addendum.*—As this article is intended more as a contribution to the history of biochemistry than a complete biography, I cannot go into the details of Lavoisier's unjust trial and execution, by the tribunal of the French Revolution in 1794. Lavoisier was guillotined with 21 others connected with the work of the *"Fermier Général."* After the execution the great Lagrange said to Delambre, *"Il ne leur a fallu qu'un-moment pour fair tomber cette tête-et cent années ne suffiront pas pour en reproduine un semblable"* (Eloge de Langrange par Delambre Mémoires de l'Institut 1812 PXIV).

## BRIEF ABSTRACTS OF IMPORTANT PUBLICATIONS OF LAVOISIER

**Experiments on respiration in animals and the changes which take place in the air passing through the lungs. (1777.) Œuvres II, 174-183.**

Of all the phenomena of animal life none are more striking and none arouse the attention of the physicist and physiologist more than those which accompany respiration. Heated mercury absorbs about ⅙ its volume from the atmospheric air by calcination, the remaining air cannot sustain respiration and combustion. On heating the mercurial precipitate we obtain a gas, which when mixed with the rest of atmospheric air again resembles the latter. A sparrow when confined in an air mass of 31 cubic inches dies in 55 minutes; the volume of air is only slightly diminished, about 1/60. The residue cannot serve respiration or combustion and renders lime-water cloudy. Caustic potash decreases the volume ⅙, loses its alkalescence, effervesces with acids and crystallizes; briefly, it has become united to "fixed air." What remains after this absorption behaves just like the air in which Hg became calcined; if the respirable portion of ordinary air be now added we again have the latter. Therefore only two things are possible, either respiration changes the "respirable air" into "fixed air" (which Lavoisier calls *acide crayeux*, because it may be developed by treating chalk with acids) or an interchange takes place. [He inclined to the latter view because "respirable air" changes the blood to a red color like the metals (Hg, Pb, Fe) in calcination, but believes that both occur.]

**No. 4, p. 537. On the combination of "fire material" (*la matière du feu*) with vaporous fluids and the formation of aeriform elastic fluids. (1777.) Œuvres II, 212-224.**

An evidence of Lavoisier's inclination to the phlogiston theory. The author is of the opinion that there exists a very fine substance which he calls "matter of fire, of heat and of light" (*matière du feu, de la chaleur et de la lumière*) which permeates all bodies, forming with them an equivalent weight, not readily penetrable by each, and that this fluid exists in part free and in others (material bodies) in combination. The supposition is not new and its admissibility is proved by the conformity of the phenomena of which he treats and the fact that it explains all experiences of physics and chemistry. As with water with which a chemical combination is conducted, for example, in adding an alkali to an acid solution to form a neutral salt, a double rôle is played, in that a portion of the same enters into the combination, the other portion taking up the salt contained in the solution, keeping the particles of the salt apart, so that each part of the fluid contains an equal portion of the salt, so with "fire material" which permeates each body, a portion of which is in combination and the other free, keeping apart the particles of the body. In bringing together different substances, and chemical dissociation or union takes place, it depends upon whether or not the new formed substances require as much "fire material" as the original; in the latter case heat must either be set free, which is noticed in the result, or it is abstracted from the surrounding bodies. Since all bodies take up "fire matter," measurements of the same cannot be determined exactly. All vessels are also lined with pores through which "fire matter" passes in, so that it cannot be measured like a fluid or gas shut off. Cooling sets in upon evaporation, as shown by Richmann, Mairan, Cullen and Baumé, and vapors are therefore produced by the union of fluids with "fire matter." Descriptions of experiments which he made conjointly with Laplace on the evaporation of fluids under the cell of the air-pump and refutation of the claims of the heat given off from limestone and effervescing alkalies by addition of acids are also given.

**Mémoires sur la combustion en général. (1777.) Œuvres II, 225-233. No. 7, p. 538. Memoirs on heat (Lavoisier and Laplace, 1780). Œuvres II, 283-285.**

This work is in four parts. In the first the terms "free heat," "heat capacity" and "specific heat" are defined.

The authors do not decide between the two hypotheses on the nature of heat; according to one it is an imponderable fluid, whilst the other asserts that it is due to oscillation of the matter. They claim, what may be true of both views, the unchangeableness of free heat by simple mixture of the bodies, whereas in chemical processes it may be increased as well as diminished. At any rate we may formulate the rule that every change of heat, whether real or apparent, occurring in any alteration of the bodily system, must appear in inverted order when that body assumes its original state. They designate "heat unity" as the amount of heat necessary to raise 1 pound of water to 1° on the scale of 80°; they term "heat capacity" or "specific heat" the relative heat units required to raise equal masses of different substances to an equivalent number of degrees. Conditions may vary in different temperatures, but it may be inferred that it is sufficiently constant within the limits of 0° to 80°. Since the admixture method is not sufficient to determine the specific heat, they show how it may be measured by means of ice, and describe the theory of development of the ice calorimeter and the apparatus employed.

In the second part the value of specific heat is considered with reference to water for a number of substances; further, the heat which is generated by mixing $H_2SO_4$ and $H_2O$, Ca with $H_2O$, Ca with $KNO_3$, the combustion of various substances and the heat developed in a guinea-pig.

The third part consists of hypothetic considerations foreign to our subject.

In the fourth part heat from combustion of coal and the amount of $CO_2$ is again estimated and compared to that produced in a guinea-pig and the air expired. The comparison of value as to conformity is sufficient to warrant the conclusion that respiration is a form of slow combustion, and similar to the burning of coal. The heat generated by the lungs is taken up by the blood and distributed throughout the body, and, like Crawford, the authors believe that the difference of heat capacity between arterial and venous blood also contributes to this. From all this they hold that the maintenance of an equal temperature in animals, with constant loss going on, is in great part due to the generation of heat by the union of the inspired "pure air" with the bases of the "fixed air" furnished by the blood.

**Nos. 11 and 12, pp. 539 and 540. First memoir on respiration in animals. (1790.) Œuvres II, 688-703. Premier mémoire sur la respiration des animaux. First memoir on respiration in animals. (1790.) Œuvres II, 704-714. Premier mémoire sur la transpiration des animaux.**

These two works of Lavoisier and Seguin give a more exact description of their former experiments on respiration and animal

heat. In the experiments of Laplace and Lavoisier the amount of heat produced in animals was found to be somewhat greater than the $CO_2$ given off. The account for this L. (1785) gave his opinion that probably some H besides C was burned during respiration. Respiration goes on in pure O and in a mixture of O and N under various conditions precisely in the same manner as in atmospheric air. N is neither absorbed nor excreted, but can be replaced by other indifferent gases. The amount of O taken up is greater in a lower temperature and is increased during digestion and muscle activity. The bodily temperature changes but little in the latter, but the pulse is accelerated in almost direct proportion to the amount of work yielded, so that other exertions, not measurable, such as recitation, composition, etc., may be determined thereby in a mechanical way. The average amount of O used by a man in 24 hours is estimated as 2 lbs. 1 oz. 1 dr., the C excreted as 10 oz. 4 dr., and the H (calculated as indirect from the superabundant O) as 1 oz. 5 dr. 51 gr. The article closes with observations on the nourishment of the working classes, regulation of heat and disturbances of weight equivalents.

For the examination of cutaneous transpiration they used an air-tight covering for the entire body, respiration being conducted by means of a tube in mouth. They differentiate between pulmonary respiration and transpiration. They surmise that carbonaceous and hydrogenous fluid is transpired in the blood of the lungs and then burned. With the $CO_2$ and $H_2O$ thus formed the water is evaporated as excreted by the blood. The latter is lung transpiration water, the former lung respiration water. To estimate these separately, water is calculated from the O and C, with the proviso that all $CO_2$ originates in the lungs or the blood whilst circulating in the vessels. The sum total of respiration and transpiration is formed by weighing before and after the experiment, and the part taken by the lungs alone by weighing by means of the apparatus before and immediately at the end of the experiment, the difference then shows the part played by the skin. The authors are not deceived by the uncertainty of this hypothesis.

A résumé of all the published work by Lavoisier was given by Seguin alone in 1814.

# ABSTRACTS OF PAPERS

**Representing Work Done in The Johns Hopkins Hospital, but Published or to be Published Elsewhere than in the Bulletin Prepared by the Authors**

## THE INFLUENCE OF ACID PHOSPHATE UPON THE ELIMINATION OF AMMONIA IN THE URINE

W. McK. Marriott and John Howland

*(From the Department of Pediatrics, The Johns Hopkins University)*

In the course of nephritis, acidosis may develop, but the evidences of acidosis differ from those usually found, in that there is no increase in the ammonia of the urine. It would seem from this that the acid responsible for the disturbance of acid base equilibrium in nephritis is different in character from those causing acidosis in other conditions.

We have previously shown that in nephritis there is an accumulation of inorganic phosphate in the blood plasma, due presumably to a failure of the kidney to excrete acid phosphate. We wished to determine, therefore, the difference, if any, in ammonia production resulting from the ingestion of acid phosphate and hydrochloric acid in equimolecular amounts.

The subjects were four normal men. Each was on his usual diet throughout the experiment which continued over 12 days. There was a preliminary period of three days. During the fourth day each subject drank 500 c. c. of decinormal hydrochloric acid. Following this there was a "normal" day. On the third day each subject took the equivalent of 500 c. c. of decinormal acid sodium phosphate ($NaH_2PO_4$). On the following day 1500 c. c. of decinormal acid sodium phosphate were taken by each subject. Two "normal" days followed and then each subject took a solution of sodium phosphate having a pH of $10^{-7.4}$, that is, the reaction of the body, and containing exactly the same amount of $PO_4$ as the 500 c. c. of decinormal acid phosphate. On the following day 1500 c. c. of decinormal neutral phosphate were taken. A subsequent "normal" day completed the experiment.

In the table are shown the average values for some of the important factors. From the results, it appears that hydrochloric acid administration increases distinctly the ammonia coefficient in the urine and at the same time the titratable acid increases in about the same proportion, so that the $\frac{A}{NH_3}$ ratio remains essentially unchanged. On the other hand, the administration of acid phosphate equivalent in titratable value to the hydrochloric acid led to absolutely no increase in ammonia excretion, and even three times this amount (1500 c. c.) failed to increase the excretion of ammonia. There was, however, a great increase in the titratable acid of the urine that the $\frac{A}{NH_3}$ ratio increased greatly, reaching a point corresponding to that observed by Henderson and Palmer in severe nephritic acidosis. It would appear that the presence of phosphate in the body actually inhibits the production of ammonia, since hydrochloric acid alone leads to a great increase and the administration of 500 c. c. of decinormal acid phosphate is essentially the same (except for inert sodium chloride) as the administration

| | Vol. in c.c. | pH | A* | $NH_3$* | $\frac{A}{NH_3}$ | TN gms. | P gms. |
|---|---|---|---|---|---|---|---|
| Normal | 1570 | 6.15 | 262 | 381 | 0.68 | 13.5 | 0.98 |
| Normal | 2100 | 6.4 | 279 | 386 | 0.71 | 13.2 | 1.06 |
| Normal | 1250 | 5.9 | 328 | 380 | 0.86 | 13.7 | 1.08 |
| 500 c.c., $\frac{N}{10}$ HCl | 1860 | 5.5 | 404 | 529 | 0.76 | 13.5 | 1.05 |
| Normal | 1410 | 5.8 | 310 | 437 | 0.71 | 12.7 | .98 |
| 500 c.c., $\frac{N}{10}$ Acid Phos. | 1890 | 6.05 | 476 | 422 | 1.13 | 14.7 | 1.98 |
| 1500 c.c., $\frac{N}{10}$ Acid Phos. | 2400 | 5.8 | 956 | 439 | 2.17 | 13.3 | 3.91 |
| Normal | 1570 | 5.85 | 512 | 433 | 1.19 | 12.4 | 1.88 |
| Normal | 1130 | 6.1 | 273 | 358 | 0.76 | 11.8 | 1.11 |
| 500 c.c., $\frac{N}{10}$ Neut. Phos. | 1660 | 6.5 | 367 | 319 | 1.14 | 11.5 | 2.03 |
| 1500 c.c., $\frac{N}{10}$ Neut. Phos. | 1690 | 6.8 | 323 | 238 | 1.36 | 12.9 | 3.65 |
| Normal | 1860 | 6.7 | 295 | 319 | 0.93 | 12.4 | 1.81 |

*A represents the total titratable acid for 24 hours and $NH_3$ the total urinary ammonia, each expressed in c.c. of decinormal solution.

of an equivalent amount of neutral phosphate to which 500 c. c. of decinormal hydrochloric acid has been added. We should suppose, then, that the administration of phosphate at exactly the reaction of the body should decrease the ammonia excretion of the normal person and our results show this to be the case. There was a decrease in the excretion of ammonia after taking neutral phosphate and the $\frac{A}{NH_3}$ ratio became greater than that seen in the normal person.

The experiments reported show that the presence of acid phosphate in the body, even in the absence of renal disease, gives rise to the excretion of urine of a character such as has been previously observed only in nephritic acidosis. It is our opinion that these results give additional confirmation to the view that the acidosis occurring in the course of nephritis is due to the retention of acid phosphate.

## THE EFFECT OF ALKALI AND MALT PREPARATIONS UPON THE RETENTION OF CALCIUM IN INFANCY

By AKIRA SATO, M. D.

*(From the Harriet Lane Home and from the Department of Pediatrics, The Johns Hopkins University)*

This investigation was undertaken to see if an alkali has any beneficial influence upon the retention of calcium in an infant (as Dubois and Stolte (1913) reported in their article) and if carbohydrate has an unfavorable effect upon calcium storage, as some authors believe. Eight experiments were made upon the same infant with the same amount of milk as the diet. In some periods, sodium bicarbonate was added and in others, preparations of malt both with and without the alkali. The results were as follows:

The addition of an alkali produced not only no favorable effect upon the retention of calcium, but a distinctly unfavorable one, whereas malt extract alone without alkali acted beneficially upon calcium storage. Malt extract with a considerable amount of alkali produced a rather unfavorable result. It was therefore concluded that, if malt soup has a favorable effect upon calcium metabolism, it is not as a result of the alkali originally contained in it or added to it.

## A RAPID MICRO-METHOD FOR THE DETERMINATION OF PHOSPHATE AND TOTAL PHOSPHORUS IN URINE AND STOOLS

By AKIRA SATO, M. D.

*(From the Department of Pediatrics of The Johns Hopkins University)*

The method is a colorimetric one and depends upon the precipitation of phosphate by uranium. The precipitated phosphate is dissolved in acid and the color, developed by the addition of potassium ferrocyanide, is compared with that produced by the same reagent with a standard uranium phosphate solution. For the determination 0.5 mgm. of $P_2O_5$ is sufficient. Thus with the urine of the adult one would use 0.5 to 0.75 1 c. c., with the bottle-fed infant about 0.5 c. c. and with the breast-fed infant 5 c. c. But in each case a very simple test described in the original article should be made in order to determine the optimum amount of urine for the determination. The total phosphorus in the stools is determined in a similar way after digesting with sulphuric and nitric acids. In the analysis of theoretical solutions, the amount of inorganic phosphate was determined with an average error not exceeding 2 per cent. In that of urine and feces the method has yielded results differing by not more than 2 per cent from those obtained by the ordinary gravimetric method.

## AN UNUSUAL COMBINATION OF CARDIAC ARRHYTHMIA WITH ATRIAL ORIGIN OCCURRING IN A PATIENT WITH FOCAL INFECTION AND THYROID ADENOMATA

By LEWELLYS F. BARKER, M. D., and HENRY B. RICHARDSON, M. D.

**(To be published in full in The Archives of Internal Medicine)**

The paper describes a patient, aged 51, who for three or four years had presented nervous symptoms (insomnia, depression, weakness) and circulatory symptoms (dyspnœa on exertion, tachycardia, palpitation).

On physical examination he showed slight cyanosis, tachycardia, slight hypertension—blood pressure 145 systolic, 80 diastolic—eye signs of hyperthyroidism, oral sepsis, slight nodular struma, palpable liver, undescended left testicle. The blood was normal, the Wasserman reaction was negative, the stomach juice was normal, the urine showed a faint trace of albumin, but no casts. On X-ray examination there was slight clouding of the right antrum. Telerœntgenogram measurements: M. R. 6.7, M. L. 9.1. The adrenalin test showed rather marked hypersensitiveness to this substance. There was chronic tonsillitis and a moderate degree of benign prostatic hypertrophy without residual urine.

Electrocardiagraphic studies showed, at one time or another, the following: (1) Physiological rhythm; (2) dislocation of the pacemaker from the sino-atrial node to points elsewhere in the atrium; (3) alternate atrial extrasystoles, none of which provokes a ventricular response; (4) alternate atrial extrasystoles, many of which provoke a ventricular response; (5) paroxysmal tachycardia; (6) atrial flutter.

After removal of the oral sepsis, treatment of the paranasal sinusitis and a partial strumectomy, with general upbuilding measures, the patient markedly improved and the cardiac arrhythmia disappeared except for occasional extrasystoles. In the fuller report the bibliography is reviewed.

## A NOTE ON THE SUPPOSED RELATION OF THE SYMPATHETIC NERVES TO DECEREBRATE RIGIDITY, MUSCLE TONE AND TENDON REFLEXES

By STANLEY COBB

*(From the Department of Physiology, The Johns Hopkins Medical School and the Henry Phipps Psychiatric Clinic, The Johns Hopkins Hospital, Baltimore)*

**(To be published in the American Journal of Physiology, July, 1918)**

The question of the sympathetic innervation of striated muscle is still far from settled. As the evidence accumulates, the probability diminishes that a simple explanation of tonus has at last been found. For a time the researches in anatomy and physiology had made it seem probable that tonic muscular contraction was due to sympathetic innervation. In this work

some experiments of deBoer and Dusser de Barenne were modified and repeated. A series of experiments was done on frogs to test deBoer's observation that cutting the rami communicantes of the abdominal sympathetic in frogs causes a loss of tone in the ipsilateral leg muscles. Sixty-one frogs were operated on in different ways and although the simple cutting of the rami usually seemed to cause the leg to hang lower, no consistently corroborative evidence was obtained from stimulation or degeneration experiments. Seven cats were operated on. In one case simple unilateral excision of part of the abdominal sympathetic chain was performed; the abdominal sympathetic was cut before decerebration in five cases, and afterwards in one case. The effect of stimulating the sympathetic chain was tried out, also the effect of inhibiting decerebrate rigidity by cerebellar stimulation, with and without an intact sympathetic chain. Besides this, repeated observations were made on six cats, after their recovery from the sympathetic excision, to see if the muscular tonicity or tendon reflexes had been affected.

The following conclusions were reached:

(1) Section of the abdominal sympathetic chain in cats:
   (a) Has no effect on decerebrate rigidity, either by preventing its development or its inhibition.
   (b) Causes no obvious hypotonicity of the hind legs or tail.
   (c) Causes no change in the tendon reflexes.

(2) Stimulation of the abdominal sympathetic chain causes no tonic contraction of the ipsilateral hind leg.

# NOTES ON NEW BOOKS.

*History of Medicine, Suggestions for Study and Bibliographic Data.* By FIELDING H. GARRISON, A. B., M. D., Principal Assistant Librarian, Surgeon General's Office, Washington, D. C. Second edition revised and enlarged. Octavo of 905 pages with many portraits. (*Philadelphia and London: W. B. Saunders Company, 1917.*)

The appearance of the second edition of Garrison's work is an index of the increased interest which has been aroused in the United States in the study of medical history. The first edition was a distinct advance on previous histories of medicine in the English language, and served a most useful purpose here and elsewhere. The additions and changes in the second edition bear remarkable testimony to the zeal, scholarship and industry of the accomplished author. The work has been revised, enlarged and made even more useful to the student of history than before. It deserves the widest circulation and the most careful consideration on the part of all persons who take any interest in the checkered past of medicine, or who are stimulated by the review to cherish hopes for the future. The book is admirably printed, and the proof reading has been excellent. H.

*Syphilis.* By LLOYD THOMPSON, M. D. (*Philadelphia: Lea & Febiger, 1916.*)

The subject of syphilis is perhaps the most important one of all the great divisions in medicine to-day. As the author of the book aptly states this in the opening sentences of the preface, one must involuntarily agree with him; because, after all, some of the most brilliant researches and solutions of medical problems have been made by workers in this field in the past 15 years. Many of these conclusions, coupled with a more intensive study of the subject, have made us all so much more keenly alive and sensitive to this great problem that a book of this character can of a certainty lay a claim to some kind of recognition.

Books dealing with syphilis have always been available, varying from the chapter in the average text-book, devoted to syphilitic manifestations of the special field under consideration, up to the large systems which are, of course, encyclopedic in character. However, there is always a place for an up-to-date book which is concise, brief and yet sufficiently comprehensive to make it a thing for ready and satisfying reference.

This book should appeal particularly to the student because it deals quite broadly with the entire subject; and as stated, is certainly handy for reference for the busy teacher. It is very commendable that the author has given a decidedly interesting though necessarily brief history of the disease, and of the advancement of our present-day knowledge of it; and that he has added an interesting chapter on the importance of syphilis is a genuine advantage.

In one sense the book is encyclopedic in character, even though the discussions are not entirely comprehensive; but its very brevity in this respect is perhaps a real asset. The last part (III) devotes nearly 40 pages to a description and treatment of congenital syphilis—much of which is of necessity a repetition of what has gone before.

Among some of the noticeable features to which attention might be directed are the persistent references to the great importance of the Wassermann blood test—a factor which is, of course, of inestimable value, but which, if emphasized too much, might tend to discredit and to discourage a keener study of the clinical aspects of the disease—the very thing which permitted such men as John Hunter, Ricord, Fournier, Erb, Jonathan Hutchinson, etc., to become the great masters. We must never relax our clinical vigilance with a subject such as this, and should rely on laboratory tests rather as adjuvants.

There are a few minor defects in the text, such as typographical errors, in the misspelling of proper names and of drugs (asperin for aspirin), as well as in the use of terms (tubercular for tuberculous). However, the book has the decided advantage of bringing together in one volume all phases and aspects of the subject in proper co-ordination and good arrangement. Furthermore, it supplies what we consider an important essential for a text-book, namely, brief but significant additions culled from the author's personal experience.

Without taking up the various chapters, we would mention merely the excellent and clear expositions of laboratory technique; the helpful and not too numerous references as foot-notes; and the splendid, comprehensive, yet concise descriptions on pathology, especially of the skin manifestations.

The book is attractively presented, in very handy form; the photographs of the skin lesions are adequate but not unusual, and on the whole the book should become a necessary part of every medical student's library.

With the rapid advancement in our knowledge of syphilis of the nervous system, the appearance of the book is very timely. Much has been accomplished, especially in the matter of treatment, since the publication of this volume. The treatment of these manifestations is at present passing through a stage of trial, and judging from results published by various authors much is to be hoped for.

We, therefore, look forward to the appearance of a subsequent edition of this book with much anticipation and assurance.

I. R. P.

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## THE DEVELOPMENT OF THE HUMAN VERUMONTANUM


By Ernest M. Watson, A. M., M. D., Buffalo, N. Y.

*(From the James Buchanan Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, Md.)*


Our knowledge regarding the origin and more particularly the development and structural formation of the verumontanum is far from complete. In studying the literature one finds numerous references to the development of the Wolffian ducts and to the gross changes of the Müllerian ducts in their transformation to form the prostatic utricle or sinus pocularis. Beyond the mere recognition of Müller's tubercle or Müller's hillock on the dorsal surface of the urogenital sinus, however, there are practically no recorded observations on the growth and notably the developing glandular structure of the verumontanum. Accurate studies begin only with adult life.

The notation of the occurrence of a raised prominence on the floor of the posterior urethra in connection with the development of the Wolffian and Müllerian ducts was probably first made by Müller. Felix,[1] in his monograph on the Development of the Urinogenital Organs, in Keibel and Mall's System of Embryology, states: "The two excretory ducts remain close together and the region in which they open becomes raised up into a hillock and projects into the lumen of the urethra; this hillock we shall term Müller's hillock." This structure, in its later stages containing the sinus pocularis (fused Müllerian ducts of the female), the lower ends of the paired Wolffian ducts with their openings, together with various glandular tubules and inter-tubular stroma comes to form the verumontanum of later embryonic and of adult life.

Rudinger[2] and Henle[3] among the earlier writers described the gross picture of the veru quite at length. Concerning the prostatic utricle or sinus pocularis much has been written. Morgagni[4] first called attention to this structure contained within the veru and later Albinus,[5] Schlichting[6] and particularly Weber,[7] discussed in some detail its formation and especially the analogy between it and the uterus of the female.

Among the present-day writers the work of Rytina[8] on the histology and gross anatomy of the adult verumontanum is the most complete and comprehensive. Lowsley[9] in his studies on the development of the human prostate gland only briefly mentions the changing morphology of the verumontanum.

The material for this study was obtained in part from the Embryological Collection of the Carnegie Institute and in part from the Obstetrical Service and from the Pathological Department of The Johns Hopkins Hospital. In all eight human embryos were studied varying in age from the thirteenth week of fœtal life until birth. The age of each was determined according to the table and classification of measurements in Keibel and Mall's[10] System of Embryology. The specimens were embedded in paraffine and serial sections were made through the genito-urinary tract of each specimen from the urachus to the anterior urethra. These were cut in varying thickness—6 $\mu$ and 15 $\mu$ in the younger and 40 $\mu$ in the older specimens. The sections were stained in hæmatoxylin

and eosin and every section was saved for study. The measurements of the various structures were made by means of a micrometer eye-piece for the lateral diameters and for the perpendicular height by counting the several sections, each of which was of a known thickness.

### Fœtus 80.3 mm. Long (CR), 13 Weeks Old

(No. 768c, Carnegie Collection)

Just below the internal vesical sphincter at a level where the proximal end of the prostatic utricle is first encountered the floor of the urethra is practically flat, while the lumen of the urethra as a whole is oval with the greatest diameter from left to right. The utricle is first found .7 mm. below the urethral floor as an elliptical cavity, viewed in cross-section, with its long diameter extending dorso-ventrally situated midway between the common ejaculatory ducts. These three structures, utricle and ejaculatory ducts, are surrounded by a mass of undifferentiated mesenchymatous cells which is somewhat poorly defined and blends without notable differentiation with the kindred cells going to form the intertubular prostatic tissue and the urethral walls themselves. The blood-vessels at this time occupy for the most part a position along the lateral margins of the cell mass and between it and the prostatic intertubular substance.

A few sections below this picture the mid-portion of the urethral floor shows a slight mid-line elevation with a consequent furrow at the base on either side. This furrow of elevation carries with it the mucous lining of the urethra composed of three layers of epithelial cells and below the undifferentiated mesenchymatous tissue going to form the urethral walls and the intertubular substance of the prostate. At this level there are no tubules of the middle lobe of the prostate demonstrable. As further sections are studied in order along the course of the posterior urethra an additional elevation is encountered on either side of the one noted above, lifting the urethral mucous membrane and underlying mesenchyme into two ridges resembling the one just described, although it is much smaller.

At the time of encountering these additional striæ of elevation there are several tubules of the middle lobe of the prostate noted situated midway between the first described elevation of the urethra and the ejaculatory ducts. During this progress through the sections the ejaculatory ducts have notably diminished in size and become practically round while the utricle has enlarged until now its diameter is twice that of the ejaculatory ducts and is pear-shaped or triangular in cross-section with its greatest width toward the dorsal surface of the prostate. The entire three structures in their course have come to occupy a position about the center of the prostatic tissue and have seemingly pushed the middle lobe tubules upward, well toward the urethral floor, where they are seen to open on either side of the middle elevation. At this point the middle and lateral elevations of the urethral floor merge into one rounded or half-moon-shaped structure composed of undifferentiated mesenchymatous tissue covered with the mucous lining of the urethra (which consists of several layers) and enclosing at its rather broad base the prostatic utricle and ejaculatory ducts. These in their upward slanting course have now reached the urethral level or base of the verumontanum. From here the structures take an upward slanting direction and the ejaculatory ducts finally open simultaneously on the sides of the verumontanum about its middle portion well up towards its summit. The utricle continues as a closed canal for only a few sections beyond the openings of the ejaculatory ducts where it ends as a blind pouch .1 mm. below the mucous surface of the verumontanum. The veru continues for about .3 mm. beyond the last vestige of the utricle and finally fades away in three slim elevated ridges or striæ as in its origin from the floor of the urethra above.

The veru measures about .7 mm. in length in this specimen from its origin in the striæ just outside the internal sphincter to its end in the small similar folds extending down toward the membranous urethra. Its height is .4 mm. at the most prominent portion which is above and anterior to the openings of the ejaculatory ducts and where the ducts and utricle first reach the base of the veru on their upward slanting course through this organ. The width of the veru at its widest point, which is also at the site of greatest height, is .7 mm., making it of equal length and breadth at this stage. The prostatic utricle extends as a hollow tube lined with mucous cells one or two layers deep for a little over .4 mm. coursing through the prostate gland in an upward slanting direction.

The cavity of the utricle is somewhat cigar-shaped and on cross-section tends to be oval, measuring about ⅛ by 1/10 mm. in diameter. At this stage the veru is made up of a mass of undifferentiated mesenchymatous cells budding forth from the mid-ventral portion of the urethral floor and pushing the urethral mucous membrane before it. Its cells cannot be differentiated from those forming the intertubular substance of the prostate itself. There is no evidence of any tubular elements in the verumontanum as yet, but above are a few tubules of the middle lobe of the prostate which may be seen entering the urethra along the prostatic furrows sometime before the openings of the ejaculatory ducts are encountered.

The walls of the ejaculatory ducts are composed of undifferentiated mesenchymatous cells, which are as yet not unlike those going to form the substance of the veru itself. At the openings of the ejaculatory ducts into the urethra there is no suggestion of any change in the arrangement of the cells, but here the mucous lining of each duct is approximated so that the lumina of the ducts are filled in. The cells going to form the veru even at this state are more closely packed and take the stain more deeply than those of the intertubular substance of any of the prostatic lobes, a fact indicating embryologically that they are perhaps a little older or were laid down a little earlier than the prostatic stroma.

### Fœtus 105 mm. Long (CR), 14 Weeks Old

(No. 1358e, Carnegie Collection)

The three striæ arising from the urethral floor entering into the formation of the verumontanum above are less marked in this specimen. In fact, the middle elevation is the only one that can be readily recognized. At the first level of its identification, however, the tubules of the middle and two lateral lobes of the prostate and also of the anterior lobe are well formed. The urethra in this specimen is cone-shaped with its base corresponding to the floor of the urethra. The veru at this time is well formed and at its upper portion near the internal sphincter is an almost pedunculated organ in cross-section. Its upper surface is covered with a mucous membrane having several layers and continuous with that lining the urethra. Over the veru, however, this mucous covering is quite irregular in outline, dipping down in places to form notable pits and in some places forming a series of pockets which become shut off from the lumen of the urethra and appear as definite tubules of the outer portion of the verumontanum.

This irregularity is first noted at the tip of the veru, but in the succeeding sections it is seen to extend well down on either side to the prostatic furrows. The prostatic utricle is first observed at the base or urethral level of the veru as a slit-like aperture with its long diameter extending dorso-ventrally, while on either side are situated the common ejaculatory ducts. The utricle is lined with a several-celled layer of mucous cells in all respects similar to those lining the ejaculatory ducts.

About the utricle and ducts the mesenchymatous cells are a little more closely packed and somewhat more deeply staining than in other portions of the veru. The utricle and ducts continue an upward slanting course through the substance of the

veru and the ducts finally open into the urethra on either lateral aspect of the veru very near its summit. The utricle continues for a few sections beyond these openings and then ends as a blind pocket nearly .5 mm. below the mucous membrane of the veru. The utricle is about .6 mm. long in this specimen and .3 mm. in its greatest diameter, which is dorso-ventrally, while its walls are approximated throughout its entire course. From all points the utricle is essentially only a verual organ in this specimen at this stage. The verumontanum measures approximately .7 mm. long and .7 mm. in diameter in its widest portion, while its highest point is 1.3 mm. from the urethral floor.

The composition of the veru is still for the most part undifferentiated mesenchyme, while the walls of the ducts and utricle show simply a more close approximation of cells and as yet no definite musculature. The peripheral tubules are present, seven on the left side and four on the right, formed from infoldings of the mucous covering.

An interesting finding in this specimen shows the tip of the veru in its lower third securely attached to the roof or dorsal aspect of the urethra. This condition is apparently rare if not constituting a real anomaly, as it has not been observed in any of the other specimens studied.

### FŒTUS 130 MM. LONG (CR), 16 WEEKS OLD

(No. 1018, Carnegie Collection)

As soon as the internal sphincter is passed the longitudinal striæ which merge to form the upper surface of the veru are encountered. The middle fold is first noted, being somewhat longer than the other two situated one on either side of it. At the level where the striæ are first observed there are present the tubules of the middle and two lateral lobes of the prostate, but none of the anterior are seen. The middle fold increases in size in its course down the urethra and finally the lateral folds become a part of it. At the level where the veru may be said to begin the ejaculatory ducts are .5 mm. below the urethral floor with a few middle-lobe tubules between these two points. The urethra is somewhat star-shaped with the veru projecting well into its lumen. The irregularity of the mucosa covering the veru is noted again in this specimen forming well-defined pits, though this is not so marked as in the previous specimen.

The utricle is first encountered just below the urethral level and at the base of the veru as a somewhat irregular opening, but in general circular in outline measuring about .1 mm. in diameter situated .25 mm. below the surface of the veru. It is lined with mucous cells one or two layers deep. Immediately beneath the mucosa covering the veru the previously undifferentiated cells have now become more specialized and here form a well-defined covering over this organ of an early stroma-like sheath. Within this sheath are included the utricle and the two ejaculatory ducts which are still surrounded by a mass of clearly undifferentiated mesenchymatous cells. This stroma-like sheath can easily be traced down to the somewhat similar intertubular structure of the prostate gland with which its fibers are closely intermingled. Within this stroma are here encountered for the first time several tubules or gland acini which come to lie along the sides of the now well-formed verumontanum. In tracing these structures through the veru it is seen that they first occupied a position as a part of the sub-urethral portion of the prostate middle lobe and have seemingly been pushed upward to occupy their new position by the upward growth of the verumontanum. At this time also is noted the definite fibrous elements in and about the walls of the utricle and ejaculatory ducts. All tubules observed open into the urethra along the sides of the veru and in no instance have any tubules of prostatic origin been observed opening into either the utricle or ejaculatory ducts.

Through the veru the ducts and utricle pursue an upward slanting course and all assume an elliptical outline in cross-section. This is brought about to a considerable extent by the pressure from either side by the formation of the stroma-like sheath and the growth of several tubules within this enclosure. The ejaculatory ducts first occupy a position below the utricle at the upper level of the veru just beneath the termination of the superior striæ. In their course downward, however, they become separated and, before the mid-verual portion is reached, come to occupy a position on either side of the utricle. At this time the utricle appears as a longitudinal slit lined with mucous membrane and its walls approximated. It measures at this time .4 mm. in its dorso-ventral diameter.

Continuing their course upward the ducts decrease in size and finally, about the mid-portion of the veru, open through the sides of this organ very near its tip into the urethra. The utricle continues for a few sections beyond the openings of the ejaculatory ducts where it ends as a blind pouch .05 mm. beneath the mucous membrane of the veru. The utricle measures a little over .6 mm. in length in this specimen and is sword-shaped with its walls approximated and the greatest diameter extending dorso-ventrally. After the openings of the ejaculatory ducts are passed and beyond the utricle the verumontanum becomes a highly tubular organ. This is caused by the tubules of the middle lobe (prostate) seemingly pressing upward, so that some five or six of them have come to occupy a position in the veru giving it a decided honeycombed appearance in cross-section. After this has continued for some distance, these tubules of prostatic origin disappear and over the lower or inferior third of the organ only the infoldings arising from invaginations of the mucous covering are seen, while the extreme inferior portion of the veru has no tubular elements. As in the earlier specimen the veru gradually fades away into three or possibly four small but definite striæ of elevation, which are observed decreasing in prominence as they are traced down the prostatic urethra toward the external sphincter. The veru measures 1.25 mm. long and .6 mm. wide in its greatest diameter, while its greatest height is .4 mm. at the level of the openings of the ejaculatory ducts.

### FŒTUS 171.4 MM. LONG (CR), 19 WEEKS OLD

(No. 1049, Carnegie Collection)

The utricle is first encountered in this specimen fairly high up, before there is any indication of the formation of the veru or before even the superior striæ are noticed. It is observed as an irregular star-like cavity lined with a mucous membrane of several layers and with its walls approximated. It measures .4 mm. by .1 mm. in diameter in cross-section, the greatest width extending dorso-ventrally, and lies .5 mm. below the urethral floor. Just dorsal and on either side of it are situated the ejaculatory ducts which are about the same size as the utricle, but with their walls well dilated. Between the utricle and urethral mucosa are observed several tubules (six or seven of the middle prostatic lobe, the sub-urethral portion). Also in their respective areas about the urethra are noted the tubules of the anterior, and the two lateral lobes, and also those of the posterior lobe.

The intertubular substance of the prostate is here well defined as an unmistakable stroma. A few undifferentiated mesenchymatous cells still remain grouped about the utricle, but about the ejaculatory ducts the differentiation into a muscular coat is observed. On either side of the mid-line the urethral floor with its mucosa is slightly elevated for a short distance appearing as two striæ. The middle fold described in the three previous specimens is here lacking. These two striæ are soon lost in the general elevation of the mid-urethral floor by the pushing up of the veru. The stroma-like sheath marking the boundaries of the veru, mentioned in the previous specimen, is here still more strikingly shown, and within this the undifferentiated mesenchyme still persists, yet in the region about the utricle it has begun to take on a somewhat stroma-like aspect.

In following the ejaculatory ducts through the prostate they decrease in size as in the previous specimen and become elliptical in outline, their long diameter extending dorso-ventrally. The mucosa over the superior third of the veru is still somewhat irregular with moderate invaginations and pit formation. This irregularity is not so marked as in the specimens at 14 and 16 weeks, but is still quite evident. In their course through the veru the ejaculatory ducts and utricle pursue an upward, slanting path and the ducts finally open simultaneously in the mid-portion of the veru well up toward its tip. Even at this time there is scarcely to be noted a definite musculature to their walls, but merely a more deeply staining layer of cells which somewhat resemble stroma cells. The utricle extends only a few sections beyond the openings of the ejaculatory ducts where it ends as a blind pocket .05 mm. below the mucous membrane covering the veru. The utricle measures 1.2 mm. long in this specimen and runs as a sword-like canal with its walls for the most part approximated.

Beyond the openings of the ejaculatory ducts and the distal portion of the utricle the veru is made up very largely of tubular elements having their origin from the sub-urethral portion of the middle lobe. These with a relatively small amount of stroma and only a slightly irregular mucous membrane go to make up the organ. All tubules open on either side of the veru along its inferior third directly into the urethra. Beyond the openings of the ejaculatory ducts the tubules are more numerous, but in the superior or upper portion those of prostatic origin can be definitely made out. After the region of the tubules is passed the intertubular stroma of the veru continues for a short distance down the urethra as a central ridge and is finally lost in the floor of the urethra. The lateral inferior striæ were not found in this specimen. The veru at this time measures 2.5 mm. in length, .5 mm. in height and .9 mm. in width along its greatest diameter.

### Fœtus 178 mm. Long (CR), 21 Weeks Old

(No. 1171, Carnegie Collection)

In this specimen the superior striæ are present and well developed. The middle elevation is most prominent and on either side are two definite folds resembling to a considerable degree the picture seen in the previous specimen. The folds are covered with mucous membrane three- or four-cell layers deep, while the underlying stroma is seen extending well into each elevation. The utricle is first encountered .5 mm. beneath the superior striæ before the real urethral elevation of the veru is observed. It exists as a circular cavity, .4 mm. in diameter, situated just above the common ejaculatory ducts, which are here circular cavities .3 mm. in diameter. Both between the ejaculatory ducts and utricle on the one side and between the utricle and urethra on the other are observed several tubules of the prostatic middle lobe.

The superior striæ continue over the upper third of the veru in this specimen and are finally lost in the irregularities of the mucous membrane. This irregularity, as in the earlier specimens, has now become quite characteristic of the upper third of the veru. It is traced into pits and in the deeper portion to definite tubule formation. These tubules arising from the urethral mucosa occupy a position about the extreme periphery of the organ. The glands from the prostate (middle lobe), previously mentioned as lying above the utricle, are in the progress of the upward slanting course of the utricle and ejaculatory ducts gradually pushed upward until they become gland tubules of the veru itself. Here they occupy a position along the lateral walls of the organ beneath those tubules derived from the infolding urethral mucous membrane. These deeper tubules derived from the prostatic middle lobe finally open into the urethra along the lateral walls of the veru itself.

In the course through the veru, after the superior third of the organ is traversed, the utricle becomes much smaller and its lateral walls become approximated with the ejaculatory ducts situated on either side of it. All three structures are at this level elliptical in outline with the greatest diameter extending dorso-ventrally. Without further notable change the ejaculatory ducts continue their upward slanting path and finally open up on either side of the veru well up toward its tip. The walls of the ejaculatory ducts are in this specimen well defined throughout and the changing mesenchymatous cells which make up their walls are well observed by their elliptical shape and their more densely staining properties. The utricle continues as a closed canal a few sections beyond the openings of the ejaculatory ducts and there ends as a blind pocket .1 mm. below the mucous membrane covering the veru.

The utricle is cigar-shaped in this specimen and measures about 1.4 mm. in length. Below or inferior to the openings of the ejaculatory ducts the veru is made up of a few tubules having their origin from the prostatic middle lobe. These are here few in number (about five or six) and soon end by opening into the urethra along the sloping sides of the veru. The remainder of the veru is made up entirely of stroma having a mucous covering similar to the urethra itself. In tracing the veru down toward the membranous urethra it is seen to fade away in three striæ or folds which soon decrease to the level of the urethra. The veru measures 1.4 mm. long, .7 mm. high and 1 mm. in width at its widest point.

### Fœtus 221 mm. Long (CR), 25 Weeks Old

(No. 1172, Carnegie Collection)

Along the superior or upper portion of the urethra the striæ which merge to form the veru are clearly delineated as three well-marked folds. The middle elevation is the most prominent, but in all three the basal stroma extends well into the substance of the folds as a series of conical peaks. The mucous covering is here, as in the previous specimens, several layers thick and along the sides of the veru the indentations and pit-formation are well defined. In certain areas tubule formation from the invaginating mucous membrane covering is readily recognized. These tubules occupy the periphery of the organ. Beneath these structures are scattered the tubules of the sub-urethral portion of the middle lobe of the prostate which have been pushed upward to occupy a position in the substance of the veru itself.

The utricle when first encountered occupies a position entirely within the veru as an elliptical cavity .6 mm. below the surface of the urethra and measures .5 mm. by .3 mm. in diameter. The ejaculatory ducts at this level occupy a position dorsal and to either side of the utricle as irregular, somewhat star-shaped cavities lined with mucous membrane. The stroma at this stage is very prominent in the structure of the veru, surrounding all tubules and forming a well-defined capsule about the utricle and ejaculatory ducts. Within this capsule there still remains a small amount of poorly differentiated mesenchyme, but that entering into the formation of the walls of the ducts and utricle has very nearly the appearance observed at birth.

In this course through the veru the utricle and ejaculatory ducts become considerably elongated or elliptical in cross-section and all three structures finally come to lie parallel with their long axes extending dorso-ventrally. At this time is noted for the first time an evagination and pit-formation from the walls of the utricle and to a very slight extent from those of the ejaculatory ducts also. This irregularity of their mucous lining gives these structures a definitely pocketed appearance in cross-section. A little beyond the level of this irregularity of their lining the ejaculatory ducts are seen to open on the sides of the urethra well up toward its tip. Their mouths are wide open with no suggestion of any sphincteric fibers at their orifices. The utricle extends a few sections beyond the openings of the ejaculatory ducts, but

there ends as a blind pouch .05 mm. beneath the mucous covering of the veru.

In this specimen is observed the pointed evagination of the ventral surface of the utricle toward the urethral lumen, directing its subsequent path of opening into the urethra. The utricle measures .5 mm. in length by .1 mm. in diameter at its greatest width and is confined entirely as a closed cavity within the veru. Beyond the openings of the ejaculatory ducts the veru is made up of several tubules of prostatic origin, which open along the sides of the urethra. These are surrounded by an abundance of intertubular stroma which is supplied with numerous blood-vessels. After the tubules are passed, the stroma with its rich blood supply makes up the entire verual elevation. The veru finally diminishes into three slight but definite folds, the inferior striæ, which gradually reach the urethral level toward the membranous urethra. The veru measures at this time 2 mm. long, 1 mm. high and 1.7 mm. wide.

### FŒTUS 276 MM. LONG (CR), 31 WEEKS OLD

(No. 7, Obstetrical Service of The Johns Hopkins Hospital)

The three superior longitudinal striæ are encountered at their beginning just below the internal sphincter in this specimen. They are covered with several layers of mucous membrane and, as in the previous specimen, the stroma extends well up into each elevation. Close beneath the striæ are several tubules of the middle prostatic lobe which later appear in the veru itself, well separated from the other middle lobe tubules. In following the sections down through the prostatic urethra the superior striæ are soon lost in the general elevation of the veru, which here is composed of numerous tubular nests closely bound around with stroma. All of the above-mentioned tubules open along the sides and a few at the summit of the veru.

The utricle first appears as a circular cavity 2.5 mm. below the surface of the veru and is .3 mm. in diameter. It is situated between the ejaculatory ducts which are quite irregular in outline and are approximately half the size of the utricle itself. The superior or upper third of the veru is composed very largely of the tubular elements derived from the infolding mucous membrane covering the veru, and its ventral surface is above extremely irregular owing to this infolding and pit-formation of the invaginating mucosa. In its course through the prostate the utricle increases in size and becomes irregular while the ejaculatory ducts on either side rapidly diminish in diameter and tend to become circular in outline.

When first observed the utricle and ejaculatory ducts are clearly walled off within a very definite stroma capsule and this persists about these structures during their course through the prostate gland. The sub-verual structures become thinned out in this specimen and the veru and utricle seem to approach each other by a thinning out of the intermediate tissue more than by a course through the prostate. At this level the few middle-lobe tubules, which eventually become a part of the verual gland tissue, are easily recognized and appear just above the utricle and are literally pushed up by it to their new position in the veru. The peripheral verual tubes from their origin from the infolding of the urethral mucosa are here well separated from the tubules of prostatic origin by a well-defined area of stromal tissue.

In tracing the varied structures through the veru the utricle is seen to become quite irregular in outline and in places almost star-shaped in cross-section. The evaginations from its main walls to form tubules are few, less numerous than in the preceding specimen, and are located for the most part between the utricle and ejaculatory ducts. All the structures finally open spontaneously into the posterior urethra, the utricle at the summit of the veru in the mid-line and the ejaculatory ducts on either side of the opening of the utricle. The utricle gives an almost double-duct appearance at this level by its great irregularity, possibly of significance from its origin from the paired Müllerian ducts of the female. About the openings of the ejaculatory ducts there is no evidence of any isolated fibers that might have a sphincteric action. Both orifices are free and gaping.

The opening of the utricle extends several sections further than the openings of the ejaculatory ducts. The utricle in this specimen is 3.5 mm. long. Beyond the duct openings and utricle the veru is composed of several lateral tubules of prostatic origin which soon open into the urethra through the mucous membrane of the veru. The remainder of the veru is made up of a dense stroma which is well supplied with blood-vessels. The inferior fourth of the veru is practically free from tubules of any type. The veru finally ends by decreasing into four ridges of elevation, the inferior striæ, which are lost in the floor of the urethra. The veru is 4.25 mm. long, .3 mm. high and 1.4 mm. wide at its greatest diameter.

### FŒTUS 338 MM. LONG (CR), AT BIRTH

(No. 8, Pathological Department of The Johns Hopkins Hospital)

As in the preceding specimens, the floor of the prostatic urethra in its upper portion presents essentially the same three elevations previously termed the superior striæ. The middle elevation is here the largest and all three have their origin soon after the last of the sphincteric fibers are passed. Each is covered with mucous membrane several cell layers deep, below which is the stroma extending well up into each elevation. Even at the level of the superior striæ the irregularity of the mucous covering is present and beneath the surface the definite tubules of the veru arising from this infolding or pit-formation is well demonstrated. The tubules of the middle prostatic lobe at this time are situated somewhat deeply beneath the urethral floor just above the irregular ejaculatory ducts and well separated from the first-mentioned tubules by a rather thick layer of stroma tissue.

In their course down the urethra the superior striæ soon lose their identity and become fused with the middle elevation, which then becomes the upper portion of the verumontanum. At this level the prostatic utricle is first encountered as a somewhat irregular circular aperture .2 mm. in diameter, lined with mucous membrane several cell layers deep, surrounded by numerous strands of loosely packed stroma. Beyond this is the more definite stroma capsule which contains the tubules of mucous membrane origin, some three or four on each side situated along the lateral margins of the veru. In its path through the veru the utricle becomes quite irregular, its mucous lining evaginating well into the adjacent stroma to form well-defined tubules, all of which empty into the utricle itself. The outer series of verual tubules of mucous membrane origin all empty into the prostatic urethra along the sides of the veru. At this level, the superior or upper third of the organ, the tubules of true prostatic origin (middle lobe) have not taken a place in the substance of the veru itself.

In the following sections the ejaculatory ducts are traced upward through the substance of the prostate, gradually becoming smaller, although still maintaining their rather marked irregularity of outline. In their upward course they are observed literally pushing up into the substance of the veru several tubules of prostatic origin. These later become pushed to either side of the veru and finally open up into the prostatic urethra on either side of the veru. At this level the tubules of mucous membrane origin have practically all disappeared, for they occupy for the most part only the superior third of the veru. Traversing the substance of the veru the outline of the utricle becomes more and more convoluted and its ensuing tubule formation becomes more marked so that at the level of its opening into the posterior urethra there is a veritable nest of tubules emptying into its lumen for the most part along the mid-line but to some extent also along its lateral

walls. The utricle opens into the urethra before the ejaculatory ducts and while the latter structures are still elliptical lumina on either side of the utricle lying a little less than .3 mm. below the urethral floor. From this picture the ejaculatory ducts pursue a rapid course upward toward the tip of the veru and finally open on the upper lateral walls of the organ on either side of the opening of the utricle. The utricle measures .3 mm. long and, although very irregular, tends to be sword-shaped and measures 1 mm. by .2 mm. in diameter.

At this level and in the succeeding slides the tubules of prostatic origin become more numerous and practically comprise the entire veru except for the few supporting strands of intertubular stroma. This picture continues for only about the third quarter length of the veru, after which a mass of stroma tissue comprises the remaining or last quarter length of the organ with only a rare tubule opening along its lateral margin. Finally, the veru fades away into three rather ill-defined elevations or striæ, which eventually become lost as they approach the level of the urethral floor in the direction of the external sphincter. The veru in this specimen is nearly 4 mm. long, 1 mm. high and 1.5 mm. wide in its greatest width.

## SUMMARY

(1) At the thirteenth week of fœtal life the verumontanum is merely a rounded elevation arising from the posterior urethral floor. It is composed of undifferentiated mesenchymatous cells and covered with mucous membrane. Three striæ merge above to form its elevation and the same number are encountered below at its termination. It has no tubular elements and measures .7 mm. in height and the same in breadth at its widest portion. It contains the prostatic utricle and the terminal portions of the ejaculatory ducts.

(2) By the fourteenth week definite glandular tubules of the veru have appeared, arising from invaginations of its mucous covering and occupying a definite position about the periphery of the organ. These tubules open into the posterior urethra. The prostatic utricle is contained entirely within the veru in this specimen.

(3) A second group of tubules of the veru appear by the sixteenth week. These are prostatic in origin, arising from the suburethral portion of the middle lobe. They occupy a position just below the outer strata of peripheral tubules and all open into the urethra along the middle third of the veru.

(4) The nineteenth week of fœtal life brings no material change in the character of the elements entering into the formation of the veru other than observed in the preceding specimens. The tubules of prostatic origin are, however, more numerous.

(5) At the twenty-fifth week the peripheral tubules arising from the invaginating mucous membrane and also the middle strata tubules of prostatic origin are readily identified. In addition irregularities of the walls of the prostatic utricle and to some extent of the ejaculatory ducts are observed, with tubule-formation from the evaginating lining of the utricle.

(6) The utricle opens into the posterior urethra at the summit of the veru between the twenty-fifth and thirty-first week. At the later date the three groups of tubules entering into the formation of the veru are clearly identified.

(7) At birth the veru measures 4 mm. long, 1 mm. high and 1.5 mm. in width. It is a highly glandular organ and the three sets of tubules, (a) those about the upper portion and periphery arising from the invaginating urethral mucosa, (b) those situated in the middle and lower portion arising from the prostatic middle lobe, and (c) those about the utricle arising from the evaginating mucous lining of the utricle are easily recognized. It contains also the terminal portions of the ejaculatory ducts and the prostatic utricle.

My thanks are due Dr. Hugh H. Young, director of the James Buchanan Brady Urological Institute, for the unlimited laboratory privileges extended; to Dr. George L. Streeter, of the Embryological Department of the Carnegie Institution of Washington, for the generous supply of material, and to Dr. Charles W. Bethune, of the Sisters' Hospital, Buffalo, for his painstaking care in making the photomicrographs.

## BIBLIOGRAPHY

1. Felix: Human Embryology. Keibel and Mall, 1912, Vol. 2, p. 752.

2. Rüdinger: Zur Anatomie der Prostata des Uterus Masculinus und der Ductus Ejaculatorii. Festschrift des Aerztl. Vereines, München, 1883, 47-67.

3. Henle: Handbuch der Systematischen Anatomie des Menschen. Braunschweig, 1866.

4. Morgagni: Adversaria Anat., LV, Anat. IV, Animad. 3.

5. Albinus: Annotat. Acad. IV, Tab. III, Fig. 3, p. 25.

6. Schlichting: Syphilidos Mnemosynon Criticum. Amst., 1646.

7. Weber: Annotationes Anatom. et Physiol. Programm zu D. E. Kratzachmar's Disput. Inaug. Circa Lineamenta Physiologiæ Morborum, Leipzig, 1836. Zusätze zur Lehre vor Baue und die Verrichtungen der Geschlechtsorgane, 1846.

8. Rytina: The Radical Removal of the Verumontanum. Jour. A. M. A., 1915, LXIV, p. 45. The Verumontanum, with Special Reference to the Sinus Pocularis: Its Anatomy, Histology and Physiology. The Jour. of Urology, 1917, I, No. 2, p. 299.

9. Lowsley: The Development of the Human Prostate Gland. With Reference to the Development of other Structures at the Neck of the Bladder. Amer. Jour. Anat., 1912, XIII, No. 3, p. 299.

10. Keibel and Mall: Human Embryology, 1912, Vol. I, p. 180.

## DESCRIPTION OF PLATES

Fig. 1.—Spec. No. 768c, Carnegie Collection. Fœtus 80.3 mm. long, 13 weeks old. Transverse section through the upper limit of the verumontanum. A. Central superior stria. B. Tubules of the prostate gland (middle lobe).

Fig. 2.—Spec. No. 768c, Carnegie Collection. Fœtus 80.3 mm. long, 13 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts opening into the prostatic urethra. No inherent glandular tubules are noted at this stage.

Fig. 3.—Spec. No. 1358e, Carnegie Collection. Fœtus 105 mm. long, 14 weeks old. Transverse section through the upper portion of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Early invagination of the mucous covering to form the peripheral tubules.

Fig. 4.—Spec. No. 1358e, Carnegie Collection. Fœtus 105 mm. long, 14 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Fibrous strands firmly attaching the tip of the veru to the roof of the urethra (an anomaly). D. Peripheral gland tubules of mucous membrane origin.

Fig. 5.—Spec. No. 1018, Carnegie Collection. Fœtus 130 mm. long, 16 weeks old. Transverse section through the upper portion

FIG. 1.

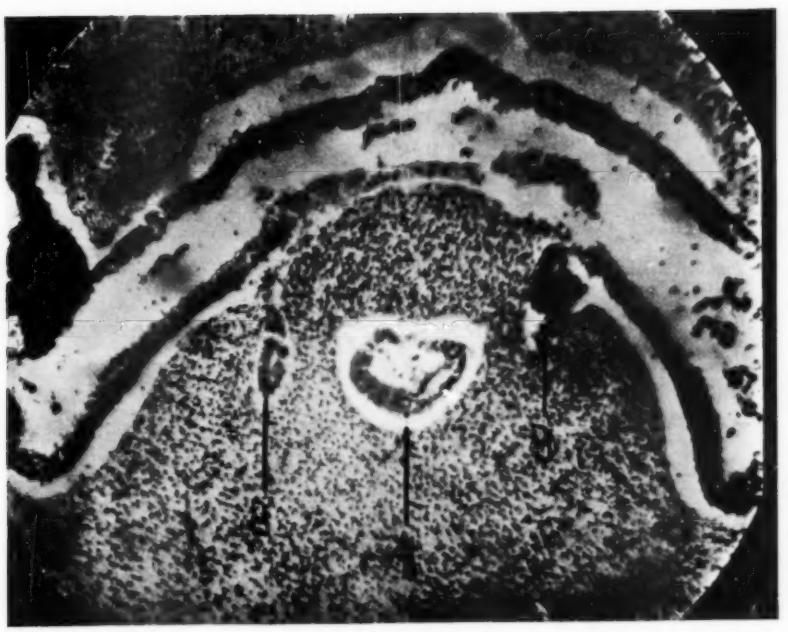

FIG. 2.

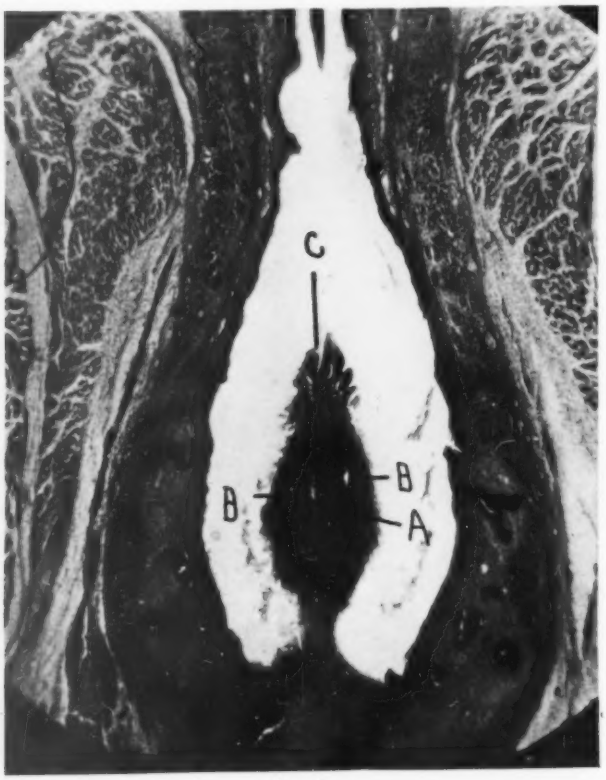


FIG. 3.

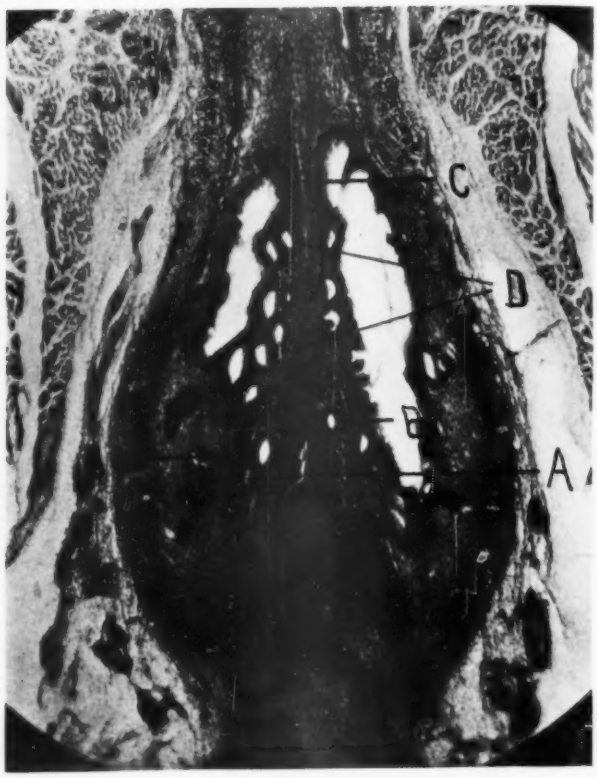


FIG. 4.

FIG. 5.

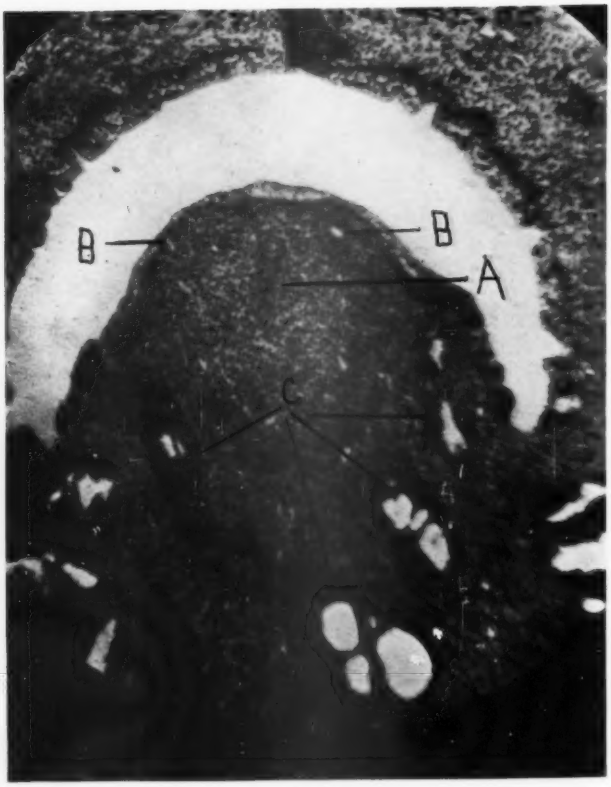


FIG. 6.

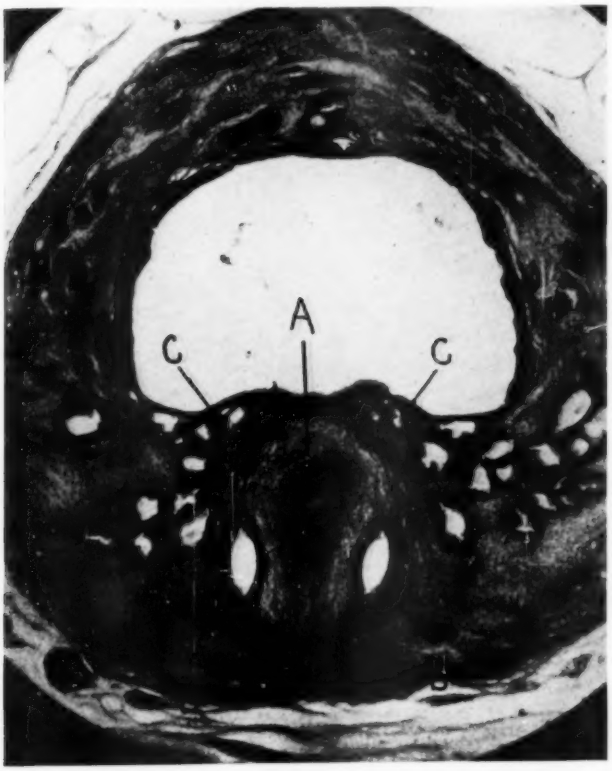


FIG. 7.

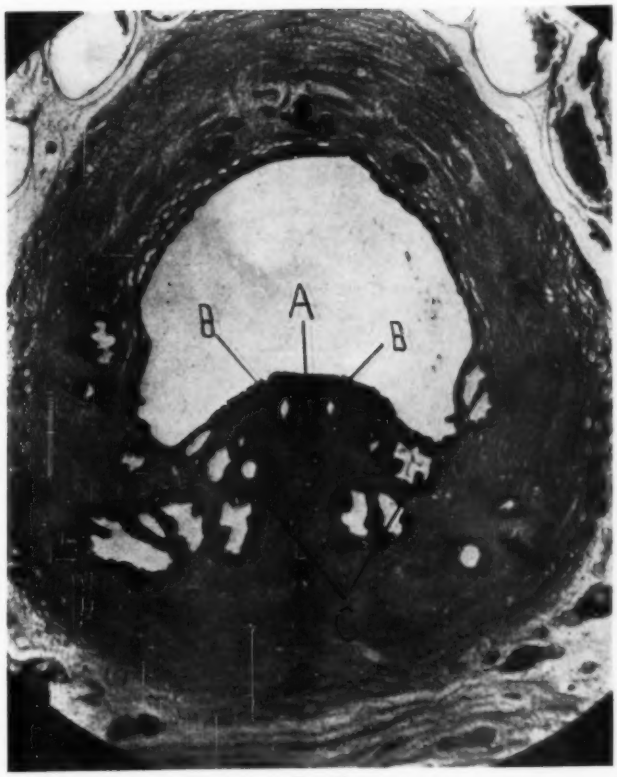


FIG. 8.

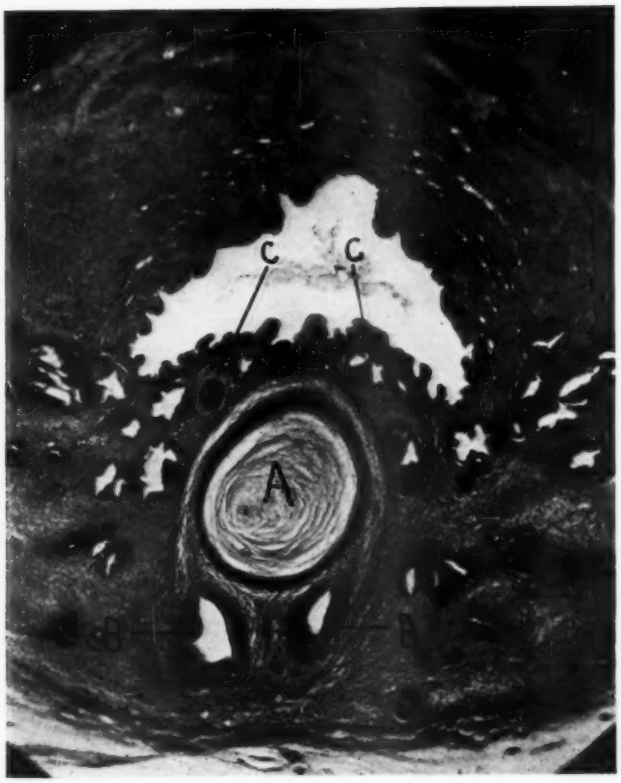


FIG. 9.

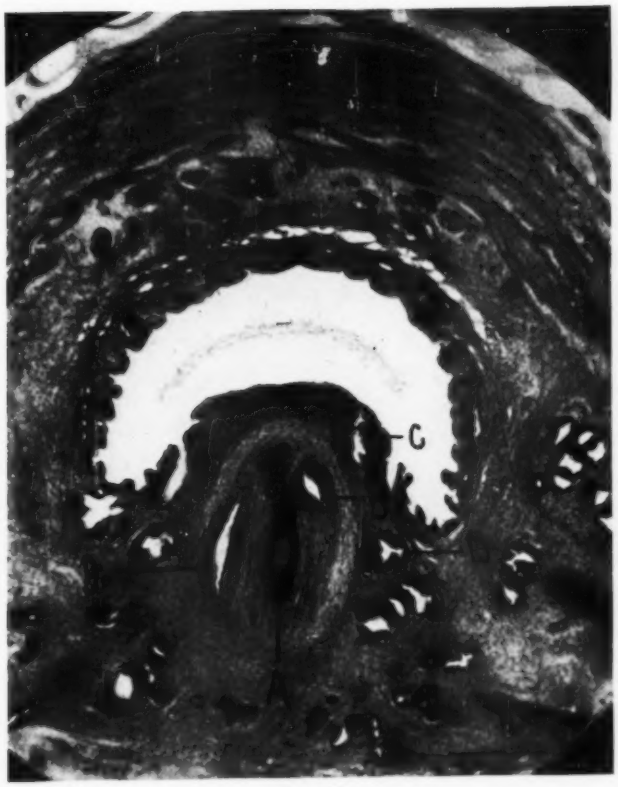


FIG. 10.

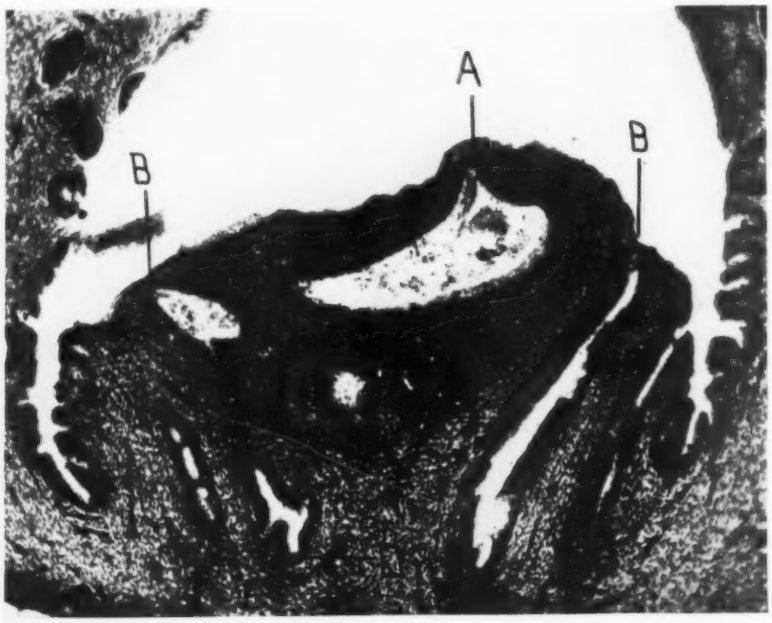


FIG. 12.

FIG. 11.

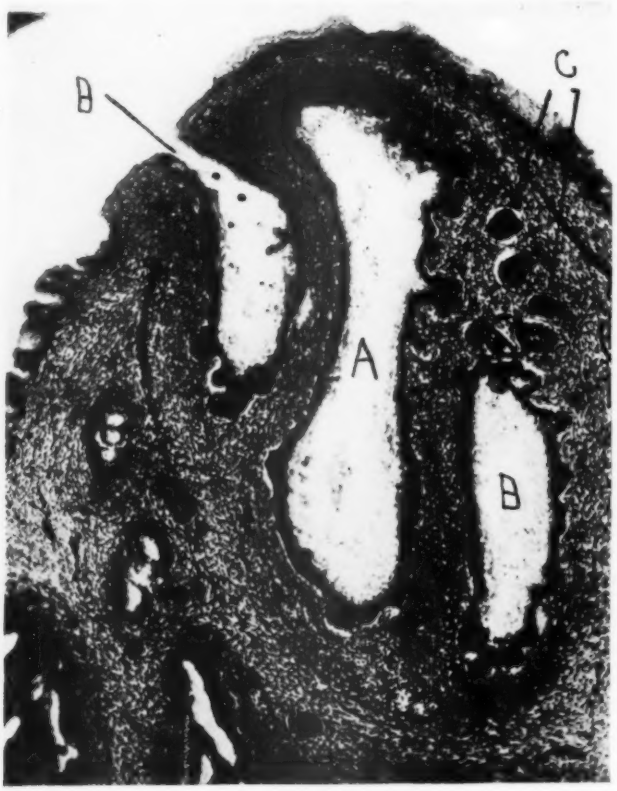


FIG. 13.

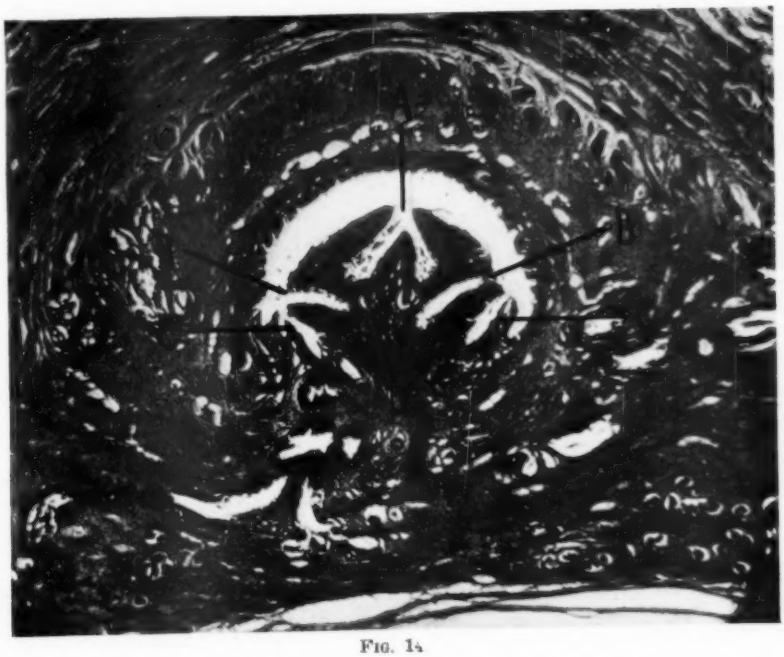


FIG. 14

FIG. 15.

FIG. 16.

of the verumontanum. A. Undifferentiated mesenchyme of the veru. B. Peripheral tubules of mucous membrane origin. C. Pitting of the mucous covering to form tubules.

FIG. 6.—Spec. No. 1018, Carnegie Collection. Fœtus 130 mm. long, 16 weeks old. Transverse section through the lower third of the verumontanum. A. Prostatic utricle. B. Opening of the common ejaculatory ducts into the urethra. C. Gland tubules of prostatic origin (middle lobe) entering into the base and subperipheral portion of the veru.

FIG. 7.—Spec. No. 1049, Carnegie Collection. Fœtus 171.4 mm. long, 19 weeks old. Transverse section through the upper portion of the verumontanum. A. Prostatic utricle surrounded by a beginning stroma-like sheath. B. Common ejaculatory ducts. C. Gland tubules of mucous membrane origin.

FIG. 8.—Spec. No. 1049, Carnegie Collection. Fœtus 171.4 mm. long, 19 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Gland tubules of prostatic origin (middle lobe).

FIG. 9.—Spec. No. 1171, Carnegie Collection. Fœtus 178 mm. long, 21 weeks old. Transverse section through the upper portion of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Gland tubules of mucous membrane origin.

FIG. 10.—Spec. No. 1171, Carnegie Collection. Fœtus 178 mm. long, 21 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Gland tubules of mucous membrane origin. D. Gland tubules of prostatic origin (middle lobe).

FIG. 11.—Spec. No. 1172, Carnegie Collection. Fœtus 221 mm. long, 25 weeks old. Transverse section through the tip of the verumontanum. A. Prostatic utricle showing the irregularity of its lining membrane. B. Common ejaculatory ducts showing the irregularity of their walls. C. Gland tubules of mucous membrane origin.

FIG. 12.—Spec. No. 1172, Carnegie Collection. Fœtus 221 mm. long, 25 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle pointing its subsequent path of opening into the urethra. B. Common ejaculatory ducts. C. Gland tubules of utricular origin, formed from the evagination of the walls of the utricle. D. Gland tubules of prostatic origin.

FIG. 13.—Spec. No. 7, J. H. Hosp. Obstet. Service. Fœtus 276 mm. long, 31 weeks old. Transverse section through the upper portion of the verumontanum. A. Prostatic utricle. B. Common ejaculatory ducts. C. Gland tubules of mucous membrane origin. D. Gland tubules of utricular origin.

FIG. 14.—Spec. No. 7, J. H. Hosp. Obstet. Service. Fœtus 276 mm. long, 31 weeks old. Transverse section through the middle of the verumontanum. A. Prostatic utricle opening into the urethra. B. Openings of the common ejaculatory ducts. C. Opening of a gland tubule of prostatic origin. D. Gland tubule of utricular origin, later opening into the prostatic utricle.

FIG. 15.—Spec. No. 8, J. H. Hosp. Path. Service. Fœtus 338 mm. long, at birth. Transverse section through the tip of the verumontanum. A. Opening of the prostatic utricle into the urethra with tubules entering it in the mid-line. B. Common ejaculatory ducts. C. Gland tubules of utricular origin. D. Gland tubules of prostatic origin (middle lobe). E. Tubule of mucous membrane origin.

FIG. 16.—Spec. No. 8, J. H. Hosp. Path. Service. Fœtus 338 mm. long, at birth. Transverse section through the lower portion of the verumontanum beyond the openings of the utricle and ejaculatory ducts. A. Openings of peripheral gland tubules of mucous membrane origin. B. Gland tubules of prostatic origin (middle lobe).

# ELECTROMYOGRAPHIC STUDIES OF CLONUS

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Clonus has been studied graphically by many investigators, but their results have not been uniform because mechanical methods were relied on until the introduction of electromyography. In the present work a few cases were studied intensively by means of the string galvanometer and the results seem to show that clonus gives a typical electromyogram, the details of which perhaps throw light on the nature of clonus. Beginning slowly, the periods between contractions soon shorten to a constant length, and this periodicity then varies not at all with fatigue, and only slightly with change of muscular tension. Clonus was kept up for half an hour in one case. In different individuals the average length of these periods varies only by a few hundredths of a second, the shortest being .12 second and the longest .17 second. From the theoretical standpoint the coincidence of this rate of clonus with the rate of other organic tremors brings to mind interesting speculations in regard to the nature of intrinsic neuro-muscular rhythms.

## LITERATURE

The study of clonus by graphic methods dates as far back as 1880, when Alexander James [10] recorded the contractions mechanically. In the next few years Horseley,[9] Gowers,[6] and MacWilliam [13] did similar work, using either levers or tambours connected with the moving foot. All of them report the rate of clonus to be between seven and ten per second, except MacWilliam, who records one case with a rate of 14. Examination of his records, however, shows that the waves are in pairs, and he himself states that this fast rate was recorded with the tambour attached directly to the contracting muscle, whereas the foot was vibrating simultaneously at a rate of seven. This 14 rate, therefore, is evidently an artefact due to the mechanical arrangement of the tambour.

In the years 1904-1907, four other investigators repeated and enlarged upon this earlier work. Their interest hinged largely on the making of a differential diagnosis between "hysterical" and "true" clonus. In their cases of true clonus the rate averaged between five and seven per second. Claude and Rose [3] found that six per second was the usual rate. Axenfeld [1] called it six or seven and found that Jendrassik reinforcement increased the rate. Levi [12] worked on 15 different individuals and found the usual rate to be six or seven, with one case as low as five per second. He states that fatigue increased the rate. His studies on clonus in normal and in hysterical individuals showed that they gave a much more irregular curve than that registered by the organic cases. Eshner [5] also found the rate in organic cases to vary between

5.8 and 8.0 per second, and showed that reinforcement increased the rate.

In the last few years three workers have applied the string galvanometer to this study. Wertheim Salomonson [15] examined several cases of organic disease and made simultaneous electromyographic and mechanical records, which show that the electrical discharge comes at the beginning of the muscular contraction. He found the rate of ankle clonus to be about eight per second, and shows a most interesting record of an hysterical clonus in which there is a continuous tetanus-like series of small waves underlying the larger waves that appear with the clonic muscular contraction.

Gregor and Schilder [8] made electromyograms of the muscular contractions in many forms of nervous disease; among others they show records of patellar and ankle clonus. These are at the rate of 7 to 9.5 and some of the individual contractions give several small action-currents. They mention this point as characteristic, thereby differing from Salomonson [16] who says that there is but one action-current for each clonic contraction. In an earlier paper [7] they had stated that there was but one "impulse" for each clonic contraction. All three of these authors speak of the action-currents as synonymous with the "Innervationsimpulse," an interpretation taken from Piper [14] who did the pioneer work in electromyography.

## METHOD

The apparatus used for recording the action-currents of the muscles studied was the string galvanometer designed by Dr. H. B. Williams and manufactured by C. F. Hindle & Co. This is a standard machine such as is used in "heart stations" for electrocardiographic work. The optical system and recording camera were also the stock type made by this company, except that a special gear was introduced to give greater speed to the film; with this addition a speed of from 20 to 27 cm. per second was obtainable. For electromyographic work of this kind any string galvanometer might be used with slight adaptation; descriptions of such modifications are given by Williams,[18] Snyder [17] and Forbes.[4] The string used was the one supplied with the apparatus and consisted of a gilded quartz fiber 3 micra in diameter with a resistance of 5000 ohms.

Electromyography, or the study of the action-currents of the skeletal muscles, has been described from the physiological standpoint by Piper,[14] but a short description of the method as applied to the study of clonus may be inserted here:

In order to record the electrical changes in a contracting muscle a continuous circuit must be established through that muscle and the string of the galvanometer; thus there must be two electrodes on the body surface, one connected with each end of the string. One of these is applied to the skin just over the belly of the muscle to be studied, and the other is placed over some nearby skin area beneath which there is no muscular contraction. For example, in studying ankle clonus, one electrode is placed over the belly of the gastrocnemius and the other in the popliteal space. In patellar clonus one is over the rectus femoris about 20 cm. above the patella in the mid-line, while the other is fastened to the inner side of the leg about 6 cm. away, over a spot where no muscular contraction takes place during patellar clonus. In this way action-currents of the clonus are alone recorded.

In studying ankle clonus the subject lay prone with the knee-joint fully extended. The skin was washed with soap and water, dried with ether, and the electrodes were then applied to the points designated above. These electrodes were of the non-polarizable type described by Piper [14] and by Forbes.[4] They consist, briefly, of funnels filed off at the small end so as to admit a rubber stopper; a piece of cat's bladder is stretched over the larger end, and a zinc rod is thrust through the rubber stopper into the cell which is filled with a saturated solution of zinc sulphate. The leads from the galvanometer string are attached to these zinc rods and the solution, permeating the animal membrane, makes the necessary electrical connection with the body of the patient.*

With the patient in position and the skin prepared, the electrodes are firmly fastened to the appropriate spots with narrow roller bandages. The galvanometer is then set with the string at such a tension that 1 millivolt causes a deflection of 1 cm. on the record. The connections are made with the patient; the resistance of the patient is measured and compensated, and the camera and lights are arranged for the making of the record. Then an assistant sets up ankle clonus by pressing sharply on the ball of the foot. In the case of patellar clonus the procedure is the same except that the patient lies supine and pressure is exerted on the patella to set up contractions in the rectus femoris.

When stimulation was kept up over a long period of time, as in the fatigue studies, it was found that the assistant became tired before the clonus, so it was necessary for the galvanometer operator to change places with him every five or ten minutes. This gave a short hiatus in the continuity of the clonus, but not of long enough duration to admit of much recovery from fatigue.

In some experiments the effect of a light pressure on the ball of the foot was compared with that of strong pressure. No accurate quantitative measurement of these variations in stimulation was attempted because only the grosser variations seemed to cause any corresponding changes in the periodicity, rate, and size of the action-current.

In relation to the leaking out of the zinc sulphate solution from the electrodes an interesting artefact was noticed which has been considered as possibly a physiological manifestation by Wertheim Salomonson.[15] In his records of clonus, he noticed that sometimes there was a slow wave following the quick action-currents. In the present experiments it was found that such slow curves always appeared when the solution leaked out of the electrode, allowing the membrane to

* The leaking out of the zinc sulphate solution was often troublesome. An easy way to overcome this was devised by placing a funnel of slightly larger size tightly over the completed electrode and filling in the space between the two funnels with celloidin, thus effectively sealing up the loose connection between the cat's bladder and the inner funnel.

retract slightly from the skin and thus to cause a change of contact with each movement of the underlying muscle. Accurately applied electrodes would give no slow waves at the beginning of an experiment, but during the next 15 minutes there would be a gradual appearance of such waves coincident with the leakage from the electrode (Fig. 1).

FIG. 1.

In this figure the upper tracing shows an electromyogram taken with the electrodes in firm contact with the skin (Table IX, Film 3). The lower tracing was made 11 minutes later with electrodes unchanged except for leakage of zinc sulphate (Table IX, Film 9).

## OBSERVATIONS

By the method described above, five patients were intensively studied; two of these had patellar clonus alone, two had ankle clonus alone, and one had both patellar and ankle clonus. The results of these observations are arranged below in nine tables.

The first patient, H. A., was a boy of 16 with a right-hemiplegia for 13 years. The initial lesion was probably an embolus. During the last two years he had been having epileptiform convulsions. The right leg showed both ankle and patellar clonus and both the right arm and right leg showed extensor weakness. Babinski's sign was present on the right.

The next patient, J. M., was a boy aged eight, admitted March, 1918, for broncho-pneumonia. In June, 1914, he was admitted in a delirium; he was found to have typhoid fever and bilateral ankle clonus without Babinski's sign. In July of that year he had a period of psychotic behavior. In 1916 he had rheumatic fever, and in November, 1917, he came back with choreiform twitchings that were thought to be habit spasms. The clonus was more marked in 1918 than at any time previously observed.

The third patient, R. P., male, aged 40, had phthysis 11 years ago, and eight years ago headaches with loss of sphincter control and weakness of the right leg. For the last five years he had had unconscious attacks. A diagnosis of cerebrospinal syphilis was made on the laboratory findings. There was slight weakness of the right leg with ankle clonus and a positive Babinski.

E. L. was a boy of 14, whose illness began six months ago with drowsiness, unsteady gait, and incontinence. From the physical examination a diagnosis of cerebellar tumor was made and an exploratory operation was performed. The tumor was not located, but great intracranial pressure was relieved. The patellar clonus which was present in the left leg before operation disappeared thereafter.

M. S. was a woman of 40, who had had pain in the arms and legs for five years, with staggering, ataxia, and slight bilateral spasticity for one year. There was hypertension and the fundi showed extensive arteriosclerosis. Both legs showed patellar clonus, slight ankle clonus, and Babinski.

In arranging these tables, the time at which each record was made is placed in the first column. In the second column is the number of the film. The third column is headed "Periodicity." This signifies the length of time elapsing between the beginning of one contraction and the beginning of the next in a clonus series. It is taken for granted that the appearance of the first wave in the electromyogram of a contraction bears a constant relation to the beginning of the mechanical contraction of the muscle. Simultaneous mechanical and electrical records made by Salomonson[18] show the reliability of this criterion. In recording the periods of the clonic contractions, each period was measured with dividers and read off against the time as registered in fiftieths of a second by the tuning-fork. If the same length of period repeated itself this was indicated by writing the number of times of the repetition above and to the right of the number. For example in Table I,

TABLE I.—ANKLE CLONUS
(H. A., March 8, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.15 | 1 | .18, .15[3], .14, .15[2] | 6.6 | 2. | 110 | 2 | |
| 3.16 | 2 | .16[3], .17, .16[4] ... | 6.2 | 1.5 | 110 | 3 | |
| 3.18 | 3 | .16[4] ..... | 6.2 | 3 | 110 | 2 | |
| 3.18 | 4 | .14[8] ..... | 7.1 | 2.5 | 120 | 3 | |
| 3.20 | 5 | .15[23] ..... | 6.6 | 2. | 120 | 3 | |
| 3.21 | 6 | .14[4], .15[5] ..... | 6.8 | 2. | 110 | 3 | |

TABLE II.—ANKLE CLONUS
(H. A., April 27, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks<br>Continued clonus from 3.16 to 3.31 |
|---|---|---|---|---|---|---|---|
| 3.16 | 1 | .16[13] ..... | 6.2 | 1.5 | 130 | 4 | Light steady stimulus. |
| 3.17 | 2 | .18, .17[11], .16[2], .17, .15. | 5.9 | 2.5 | 130 | 5 | Same stimulus. |
| 3.22 | 3 | .17, .18[2], .14[2], .16. | 6.0 | 1.0 | 145 | 5 | Light steady stimulus. |
| 3.22 | 3 | .23, .18[2], .16[4], .15[7]. | 6.4 | 2.5 | 130 | 6 | Sudden increase in stimulus during record. |
| 3.25 | 4 | .17[5] ..... | 5.8 | 1.0 | 160 | 6 | Light steady stimulus. |
| 3.25 | 4 | .20, .19, .17[2], .16, .15[3], .14, .15, .16, .18, .17. | 6.1 | 3.0 | 140 | 6 | Sudden increase in stimulus during record. |
| 3.27 | 5 | .18[2], .17[2], .18 ... | 5.6 | 0.7 | 160 | 7 | Light steady stimulus. |
| 3.28 | 6 | .15[4], .14, .15[2], .14, .15[2] ..... | 6.7 | 2.5 | 160 | 5 | Strong stimulus. |
| 3.28 | 7 | .16, .15[2], .16[6] ... | 6.3 | 2.0 | 150 | 4 | Continued strong stimulus. |
| 3.31 | 8 | .17, .16, .14[2], .15[4] | 6.6 | 2.5 | 135 | 5 | Continued strong stimulus. |

TABLE III.—ANKLE CLONUS
(J. M., March 20, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 2.35 | 1 | .16, .14, .12[11], .13[3], .13, .14[2], .13[3], .15[2], .12[6], .15. | 7.8 | 3. | 80 | 2 | |
| 2.45 | 2 | .15, .14[3], .15, .14[23]. | 7.1 | 1. | 100 | 2 | |
| 2.47 | 3 | .14, .13, .14, .12, .14[2], .12, .14, .12, .12[2], .13, .14. | 7.6 | 2. | 150 | 3.5 | A few waves between contractions. |
| 2.47 | 4 | .13[4], .12[2], .14, .12[4], .14, .12. | 7.6 | 1.5 | 150 | 3.5 | |

TABLE IV.—ANKLE CLONUS
(J. M., April 13, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.25 | 1 | .26, .16[2], .16[2] ... | 6. | 3.5 | 150 | 4 | Irregular, discontinuous clonus. |
| 3.27 | 2 | .13[2], .14, .13[3], .14, .13, .14, .13[3]. | 7.6 | 5. | 125 | 3 | Clonus regular and continuous. |
| 3.28 | 3 | .13[10]..... | 7.6 | 6. | 125 | 3 | Clonus regular and continuous. |
| 3.29 | 4 | .14, .13[7]..... | 7.6 | 6. | 125 | 3 | Clonus regular and continuous. |
| 3.30 | 5 | .13[16]..... | 7.6 | 4.5 | 125 | 4 | Clonus regular and continuous. |
| 3.31 | 6 | .13[2], .14, .13[2], .12, .14, .13[3]. | 7.6 | 4. | 110 | 2 | Clonus regular and continuous. |
| 3.32 | 7 | .13[5]..... | 7.6 | 5. | 110 | 3 | Clonus regular and continuous. |
| 3.35 | 8 | .13[9]..... | 7.6 | 3.5 | 110 | 3 | Clonus regular and continuous. |
| 3.36 | 9 | .14[10]..... .... | 7.1 | 3.5 | 110 | 3 | Clonus regular and continuous. |
| 3.38 | 10 | .13, .15, .13[3].... | 7.5 | 4. | 110 | 3 | Clonus regular and continuous. |
| 3.39 | 11 | .13[7]..... | 7.6 | 3.5 | 135 | 4 | Clonus regular and continuous. |
| 3.41 | 12 | .15, .14, .13.... | 7.1 | 3.5 | 135 | 4 | Clonus regular and continuous. |
| 3.44 | 13 | .13, .14[2], .15, .13, .15, .14, .15[2], .14.[3] | 7.1 | 4. | 135 | 4 | Clonus regular and continuous. |
| 3.46 | 14 | .13[3], .14, .13[2], .14 | 7.6 | 3. | 135 | 3 | Clonus regular and continuous. |
| 3.48 | 15 | .14[2], .13[4]..... | 7.5 | 3. | 135 | 3 | Clonus regular and continuous. |
| 3.50 | 16 | .13[1]..... | 7.6 | 3.5 | 135 | 4 | Less continuous, needs a forcible flexion every min. or two to keep it going. |
| 3.54 | 17 | .13[2]..... | 7.6 | 4. | 100 | 3 | Patient begins to complain of fatigue. |
| 3.55 | 18 | .13[3], .12[2]..... | 7.6 | 4. | 110 | 4 | |
| 3.57 | 19 | .12[3], .13[2], .13, .12, .13, .12[3], .13. | 7.9 | 4.5 | 135 | 4 | Stronger stimulus. |

TABLE V.—ANKLE CLONUS
(R. P., April 15, 1918)

| Time P. M. | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks<br>Clonus kept up from 2.35 to 2.59 |
|---|---|---|---|---|---|---|---|
| 2.35 | 1 | .21, .18, .16[4], .15[2], .14[3], .16[2], .14[2], .15[1]. | 6.6 | 3.5 | 110 | 5 | |
| 2.36 | 2 | .20, .18, .16[4], .15[9]. | 6.4 | 3.5 | 110 | 5 | Fresh stimulus. |
| 2.39 | 3 | .20[2], .16[7], .14, .15[2], .16, .17[2], .15[100]. | 6.5 | 3. | 120 | 6 | Fresh stimulus. |
| 2.42 | 4 | .22, .20, .18[2], .16[4], 15[31]. | 6.5 | 3. | 125 | 5 | Fresh stimulus. |
| 2.45 | 5 | .18[10]..... | 5.5 | 1.5 | 100 | 5 | Sample out of a 3 min. steady clonus from one stimulus. |
| 2.50 | 6 | .16[8]..... | 6.2 | .2 | 150 | 4 | Fresh stimulus at 2.48. |
| 2.55 | 7 | .16, .17[6]..... | 5.9 | .2 | 135 | 4 | Sample out of same series. |
| 2.56 | 8 | .17[11]..... | 5.9 | 1.5 | 120 | 3 | Sample out of same series. |
| 2.57 | 9 | .17[4]..... | 5.8 | 2. | 100 | 3 | Sample out of same series. |
| 2.58 | 10 | .18[4]..... | 5.5 | 1.3 | 150 | 4 | Sample out of same series. |
| 2.58 | 11 | .18, .19[2]..... | 5.3 | 1. | 165 | 5 | Sample out of same series. |
| 2.58 | 12 | .19[4]..... | 5.2 | 0.7 | 150 | 4 | Sample out of same series. |
| 2.58 | 13 | .19..... | 5.2 | 0.5 | 150 | 4 | Sample out of same series. |
| 2.59 | 14 | .16, .15[7], .16.... | 6.5 | 3. | 135 | 4 | Strong fresh stimulus. |

N. B. At 2.48 a steady pressure on the ball of the foot was begun and continued without appreciable change until the clonus spontaneously faded away at 2.58½. Then a new strong stretch was given to the muscle, starting up a new clonus at 2.59.

No. 5, the periodicity was .15 of a second for 31 consecutive contractions, this is then written .15[31].

In the next column the records of periodicity are averaged and interpolated into the rate per second of the clonus as a whole. For example, a periodicity of .15 equals a rate of 6.6 per second.

The fifth column gives measurements of the amplitude of the waves recorded on the moving film. These represent the

TABLE VI.—PATELLAR CLONUS
(H. A., March 8, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.35 | 1 | Average .16... | 6.2 | 1.5 | 150 | 2. | Two to three contractions only. |
| 3.37 | 2 | Average .16... | 6.2 | 1.5 | 140 | 2. | Two to three contractions only. |
| 3.39 | 3 | Average .16... | 6.2 | 2. | 120 | 2.5 | Two to three contractions only. |
| 3.41 | 4 | Average .155.. | 6.4 | 2. | 110 | 2. | Two to three contractions only. |

TABLE VII.—PATELLAR CLONUS
(E. L., March 16, 1918. Cerebellar Tumor)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 4.00 | 1 | .20, .20, .16.... | 5.2? | 3. | 50 | 1 | |
| 4.02 | 2 | .17, .15[7]..... | 6.6 | 1. | 75 | 2 | |
| 4.02 | 3 | .17, .15[2]..... | 6.4 | 1. | 85 | 3 | |
| 4.05 | 4 | .20..... | | 3. | 45 | 1 | |
| 4.06 | 5 | .19. .17[2]..... | 5.7 | 2. | 100 | 2 | |
| 4.08 | 6 | .18, .15[3]..... | 6.0 | 1. | 100 | 3 | |

TABLE VIII.—PATELLAR CLONUS
(M. S., March 29, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.30 | 1 | .16, .14[2], .13[3]... | 7.1 | 1.5 | 75 | 3 | |
| 3.31 | 2 | .14[2]..... | 7.1 | 3. | 60 | 2 | Followed by tetanus for one sec., then stimulus given and followed by tetanus. |
| 3.31 | 3 | .15, .14, .13[3], .12[2]. | 7.6 | 4. | 60 | 3 | |
| 2.32 | 4 | .17, .14, 12[7]..... | 8.1 | 4. | 60 | 2 | After rest of one min. new stimulus, followed by tetanus. |
| 3.33 | 5 | .13[15]..... | 7.6 | 2. | 75 | 2 | Clonus more easily elicited, end of a series recorded. |
| 3.40 | 6 | .13[6], .12[6]..... | 8. | 3. | 75 | 2 | |
| 3.41 | 7 | .13[4], .12, .10.... | 8.2 | 3. | 60 | 2 | Followed by tetanus at rate of 75. |
| 3.42 | 8 | .12[2], .10, .09.... | 8.5 | 4. | 55 | 2 | Running into irregular tetanus. |
| 3.42 | 9 | .17, .15, .13, .14, .12[2]. | 7.7 | 3. | 60 | 3 | |

magnified excursions of the galvanometer string, which in turn were caused by the action currents in the contracting muscle. Their quantitative value lies only in the fact that the tension of the string is so arranged that one millivolt causes a deflection of 1. cm., but this is again affected by the resistance of the patient in circuit, so the figures are only valuable for comparison in a series of observations in which the electrodes are left undisturbed. This is the case in each separate table.

In the sixth column is an average estimate of the rate per second of the action-current waves which go to make up the electromyogram of a single clonic contraction. Those small waves which are not considered large enough to represent an action-current are not counted. A factor of uncertainty, therefore, enters into the estimation of these rates and they must be considered as only approximate. In the next column the number of waves which go to make up the myogram of a single contraction are averaged and recorded. Here again it is difficult to decide whether a small excursion of the string is worth counting as a true wave.

TABLE IX.—PATELLAR CLONUS
(M. A., April 2, 1918)

| Time | Number of film | Periodicity | Average rate of clonus per sec. | Average amplitude of waves in mm. | Average rate of action-currents per sec. | Average number of action-currents per contraction | Remarks |
|---|---|---|---|---|---|---|---|
| 3.40 | 1 | .16[2], .13..... | 6.6 | 3. | 70 | 2 | 3 twitches followed by tetanus at rate of 70. |
| 3.40 | 2 | .16, .14, .12[2].... | 7.5 | 2. | 70 | 3 | Slight tetanus after 4 twitches. |
| 3.46 | 3 | .17, .16, .14[3], .13, .12[2]. | 7.6 | 2. | 70 | 2 | Amplitude in mm., 2-1, 5-2-1, 8-3-1-1, 5-1-2-1, 8-1, 5-1-1. |
| 3.47 | 4 | .16[2], .14[3], .13, .14, .13. | 7.1 | 3. | 60 | 2 | Followed by tetanus for 1.4 sec. at rate of 50 per sec. |
| 3.48 | 5 | .16[2], .14[2], .13,. 12. | 7.1 | 3. | 50 | 2 | Followed by tetanus for 1.3 sec. at rate of 60 per sec. |
| 3.55 | 6 | .14[93]..... | 7.1 | 1.5 | 60 | 2 | Continuous clonus started at 3.53. |
| 3.55 | 7 | .14[45]..... | 7.1 | 1. | 50 | 1 | Same steady clonus. |
| 3.57 | 8 | .16, .14[3], .13[7]... | 7.3 | 2. | 55 | 2 | New stimulus, and new clonus followed by 1.4 sec. of tetanus at rate of 50. |
| 3.57 | 9 | .14, .13[3], .14[3], .13[2]. | 7.4 | 2. | 60 | 2 | New stimulus, followed by irregular tetanus for 0.2 sec. |

## DISCUSSION

An examination of the above tables brings out several characteristics of clonic contractions. In the first place it will be noticed that the first few periods are longer than the succeeding ones and that it takes some time for the clonus to fall into a steady rhythm (Fig. 5). For example in Table V, Film 4, the first period is .22 seconds and the second is .20, followed by three periods of .18 and four of .16 before the clonus falls into its regular periodicity of .15; this is also shown in the third film of this table, where after a preliminary unsettled series, the contractions finally repeat themselves 160 times at .15 seconds. This seems to be as characteristic of patellar clonus as it is of ankle clonus (see Tables VIII and IX). It also appears that in any series of records the ones toward the end of the experiment are more regular than those at the beginning (see Table IV).

The effect of repeated clonus and of long continued clonus was also studied in relation to fatigue. Other investigators, notably Levi,[12] have stated that fatigue causes an increase in the rate of the clonus. In the present studies such was not found to be the case; in fact the phenomenon seems to be remarkably constant after the steady rate has once been reached. For example in Table IV it is seen that the rate of clonus is six per second at 25 minutes past three, reaching its steady rhythm of 7.6 per second two minutes later. After 21 minutes of continuous and steady clonus the rate is found to be slower, if anything, and at three fifty when the patient complains of fatigue the rate is still 7.6. At three fifty-seven the clonus has been continuous for half an hour and the rate is 7.9, but this is probably due not to fatigue, but to the factor next to be

discussed, namely variation in the strength of stimulus. Patellar clonus seems to be equally unaffected by fatigue: Table IX shows a rate of 7.5, in Film 2, and at the end of 17 minutes of constant clonus the rate is 7.4 contractions per second. In Table V, Films 7 to 13 show a clonus kept up for eight minutes with only one initial flexion of the ankle as a stimulus; the rate is slower at the end than at the beginning. The patient had altogether 24 minutes of clonus and began with a rate of 6.6 and ended with 6.5 per second. Thus it seems that fatigue in itself does not cause an increase in the rate of clonic contraction.

Variation of the strength of stimulus used to excite the clonus does, however, seem to affect the rate. This is well shown in Table V where the long continued clonus drops from a rate of 6.2 per second to 5.2 and then suddenly jumps to 6.5 when a strong fresh stimulus is given (Films 6 to 14). The explanation of this is as follows: at the beginning the assistant who was holding the patient's foot held the gastrocnemius strongly and steadily stretched; after two or three minutes his grip became fatigued and at the end of five minutes he admitted he was feeling tired, so there was without doubt a gradual diminution in the stimulus, corresponding to the fall in rate. When the new forcible flexion is given to the ankle at two fifty-nine the rate immediately increases from 5.2 to 6.5 per second. In Table II there are recorded experiments especially made to demonstrate this point: at first a light steady pressure was kept on the ball of the foot for six minutes, and the rate of the clonus varied between 6.2 and 5.9 per second. Then a sudden increase in stimulus was given and the rate quickened to 6.4. With the relaxation of this pressure it dropped again to 5.6 and when a continued strong stimulus was given the rate stayed for three minutes between 6.3 and 6.7. It is interesting to note in Table II, Films 3 and 4, that a sudden increase, although it quickens the average rate, first causes a few slow periods like the slow onset of an entirely new clonus.

The amplitude of the waves is the only factor that seems to keep pace with the strength of stimulus and the rate of clonus. With a strong stimulus and quick rate the electrical discharge from the muscle causes higher waves to be registered on the electromyogram than when the stimulus is weak and the rate slower. This shows well in Table II and is conspicuous in Table V. Where there is a new strong stimulus applied to the muscle the waves average from 3 to 3.5 mm. in height, but in the long continued clonus (in Films 6 to 13, Table V) a gradual decrease is shown, the last waves being only 0.5 mm. in height, increasing suddenly again to 3 with the new stimulus. Table II shows records of observations where the increased stimulus was applied while the record was being taken. In Film 3 a light steady pressure was being kept up which gave waves with an average height of 0.1 mm. The stimulus was then suddenly increased and the size of the waves immediately became 2.5 mm. In Film 4 this same thing is repeated with an increase of 300 per cent in the amplitude of the waves. Thus with an increased stimulus and quickened rate the electrical discharge seems to increase.

The 6th and 7th columns in the table show little of importance and too few cases were studied to make any general conclusions, but it may be worth noting that in patellar clonus (Tables VI, VII, VIII, IX) the individual contractions are usually made up of only two waves the rate of which average 80 per second, whereas ankle clonus showed about four waves to each contraction with an average rate of 125 per second. This suggests that patellar clonus is a simpler mechanism than ankle clonus, approximating more nearly a series of tendon reflexes. Salomonson [18] says that in true clonus there is but one action-current for each contraction, and that if two or more are found they are to be considered artefacts due to an "interference phenomenon." He believes that such interference arises when the electrodes are wrongly placed on the muscle. The presumption is that the electrodes are so placed that a single action-current is recorded more than once.[18] That groups of action-currents from a single contraction of a clonus series are not due to such an artefact is proved by recording a tendon reflex which shows a single diphasic wave (Fig. 6) and then, with the electrodes unaltered, eliciting a clonus which shows several action-currents to each contraction (Fig. 7).

A correlation of the height of the patient with his rate of clonus indicates that small size and high rate of the clonus go together. H. A. and M. S. were the smallest patients, and their average rate was 7.6, the others averaging 6.5 per second. This falls in line with the observations of Alexander James [19] who states that "the rapidity of ankle clonus is in inverse ratio to the height of the individual."

Most observers who have written on the subject of clonus have tried to differentiate sharply "true clonus" from "voluntary clonus" or "hysterical clonus."[2 13 18] Since this paper deals with only five cases, all of which are obviously "organic" it might seem irrelevant to take up the discussion of this differentiation, but in one case of patellar clonus (Table VIII) a constant tendency was noticed for the clonus to go over into a tonic cramp-like contraction (Fig. 4). This tonic contraction gives a tetanic series of waves resembling those shown by Salomonson in hysterical clonus and others shown by Gregor and Schilder [8 (Fig. 47)], where a voluntary contraction of the quadriceps muscle turns into a typical patellar clonus. The case described in Table VIII is one of spastic paraplegia with no hint of hysterical complication. The other case in this series which showed a tendency toward tetanic contractions complicating the pure clonus, in the case of J. M. (Tables III and IV). His records not only always showed several waves to each contraction, but also an occasional wave or a short tetanus was found between the clonic contractions. The fact that this is the case of post-typhoidal clonus without Babinski's sign makes one wonder if there is a possible "voluntary" component here, especially as the boy stated that he liked to balance his foot so it would jerk, and enjoyed the interest taken in him by the physicians. Because of such facts as these it seems wiser to make no sharp distinction between the "true clonus" of organic origin, and the "pseudo clonus" of hysteria. In the present state of our knowledge it is more reasonable to think of clonus as a slow, rhythmical neuro-

FIG. 2.

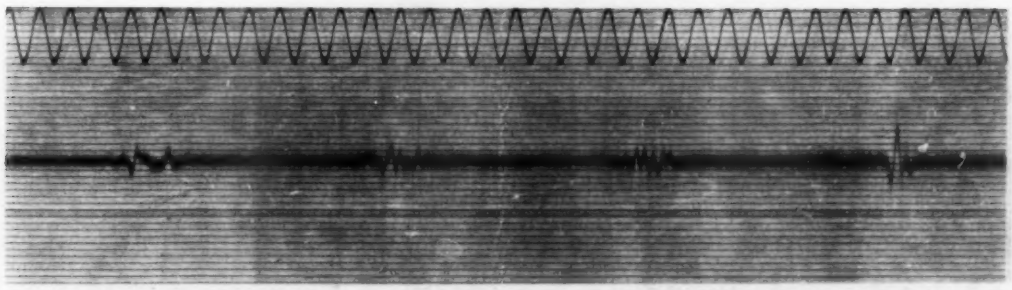


FIG. 3.

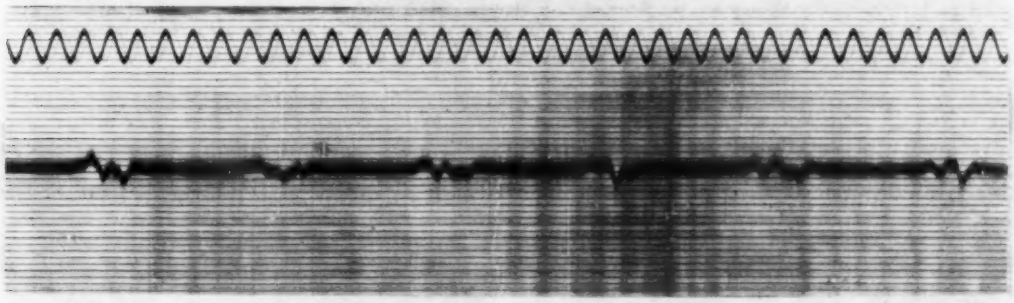
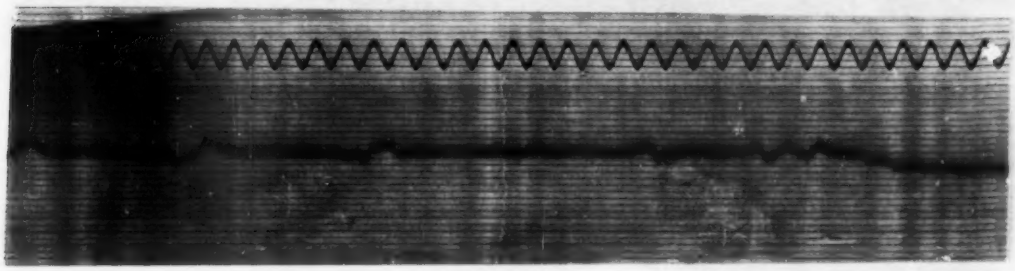


FIG. 4.



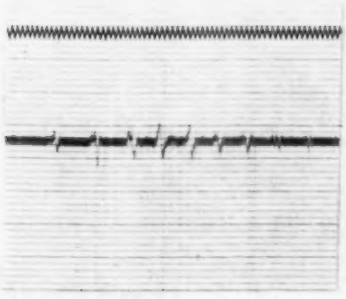


FIG. 5.

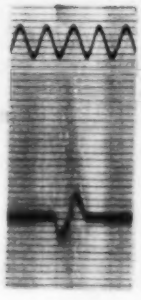


FIG. 6.

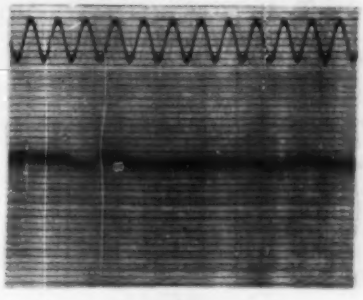


FIG. 7.

muscular phenomenon which may be more or less complicated by the faster rhythms of the psychobiologically determined "voluntary" contraction.

## THEORETICAL

There is probably no distinct line between clonic and sustained muscular contraction. Voluntary contraction is sustained, giving a tetanic electromyogram, but certain individuals can voluntarily induce a clonus. It is notable that such a clonus falls into the usual rate of about 7 per second,[1 3 10] but it is less regular than the pathological clonus studied in this paper, and it can only be elicited by people with hyperactive reflexes or after fatigue of the muscles involved.[10] In this connection it is interesting to remember that clonus is found after wasting diseases such as typhoid fever.[10] Then there is the great group of hysterical clonus which resembles the voluntary type. Only one hysterical case has been studied electromyographically,[10] but this one shows a definite tetanic (voluntary) rhythm underlying the clonus. It should be of great interest therefore to study all clonic contractions electromyographically. In this way a new diagnostic criterion might be found between hysterical and organic cases. The question would be what difference one might find in the clonus in states of normal psychobiological integration and in states of hysterical malintegration, when compared with the organic cases. In purely organic clonus there is no sign of electrical activity in the muscle between contractions. It is interesting that in the case of M. S. where the patellar clonus passes over into a tetanic spasm, the rate and the number of action-currents per contraction increases as the spasm comes on, until the tracing becomes that of a continuous contraction (Fig. 4). Illustrations of the opposite condition are shown by Gregor and Schilder [8 (Figs. 47 and 48)] where attempts at voluntary contraction of a paretic muscle give electromyograms showing transition from tetanus to clonus.

Most writers on clonus agree with Langelaan [11] who states that clonus is a reflex symptom, or a series of them; and that the stretching which follows a contraction is a new stimulus to the proprioceptors and calls forth another reflex twitch; thus the symptom propagates itself until fatigue or inhibition puts an end to it. If this were the true explanation of clonus we would expect a much shorter periodicity than that which is observed; Snyder [17] found that the reflex time of the knee jerk was about 0.011 seconds. If then clonus was purely a self-propagated proprioceptive reflex we would expect it to have a much higher rate, for in eliciting clonus we keep the muscles stretched, thus stimulating their proprioceptors, which can reflexly cause a contraction in 0.011 of a second; the muscle then relaxes only to find the stretching stimulus still there to set up another contraction. The fact that the average periodicity is 0.15 seconds when the reflex time is only 0.011 must be explained.

There seem to be three theoretical possibilities. First, it may be that the relaxation time of the muscle takes up 0.1 of a second or more. Secondly, a summation of stimuli through the proprioceptors may be necessary to cause the next contraction. And lastly central inhibition may play a rôle. The first two possibilities should be studied experimentally. For the last there is some clinical evidence already; evidence for the existence of some energy constantly tending to excite muscular contraction, but normally held in check by inhibition. Removal of this inhibition by decerebration, by central lesion, or positive motor effort, causes more or less permanent muscular contraction. There seem to be all degrees, from slight spasticity to permanent contracture, but the interesting point is that whatever the cause of heightened muscular tone may be, the rate of the clonus (or of the tremor in such diseases as paralysis agitans) falls always into approximately the same rhythm.

Piper, Salomonson, Gregor and Schilder speak of "Innervationsimpulse" when referring to action-currents in muscles, taking for granted that each action-current represents a single nerve impulse. This theory is not supported by the more recent investigations of Forbes and Rappleye [5] who have shown that warming and cooling the muscle changes the rate of its action-currents. They conclude (p. 254) that "the rhythm observed in muscle response is not the rhythm of motor nerve impulses, but is dependent, as Buchanan maintains, on the condition of the muscle." Action-currents therefore, must be looked upon as electrical concomitants of neuromuscular activity, their rate and character being controlled not only by the rate of the nerve impulse, but also by the physiological state of the muscle itself.

In closing I wish to express my appreciation to Messrs. L. S. Chapman and P. R. Holtz for their help in making the galvanometric records. I also wish to thank Dr. Meyer for his interest in the work, and the other physicians of the hospital who gave me the opportunity to study their cases.

## CONCLUSIONS

(1) Electromyography is a more accurate and more easily applied method for the study of muscular phenomena than those formerly applied to clinical observation.

(2) Clonus gives a characteristic electromyogram.

(3) Fatigue does not affect the rate of clonus.

(4) Increased stimulus increases the rate of clonus and the size of the electromyographic waves, but does not change the rate of the action-currents.

(5) The number of action-currents per contraction varies with the type of the clonus.

## BIBLIOGRAPHY

1. Axenfeld: Arch. di Fisiol., 1907, IV, 160.
2. Claude and Rose: Rev. Neurol., 1906, XLV, 829.
3. Eshner: J. Am. M. A., 1904, XLII, 1202.
4. Forbes and Gregg: Am. J. of Physiol., 1915, XXXVII, 118.
5. Forbes and Rappleye: Am. J. of Physiol., 1917, XLII, 228.
6. Gowers: Man. Dis. of the N. S., 1893, 2d edition, II, 17.
7. Gregor and Schilder: Münch. Med. Woch., 1912, LIX, 2851.
8. Gregor and Schilder: Ztschr. f. d. g. Neurol. u. Psych., 1913, XIV, 359.
9. Horsley: Brit. M. J., 1885, I, 112.
10. James: Edin. M. J., 1880, XXVI, 135.

11. Langelaan: Neurol. Centralbl., 1904, XXXIII, 1140.
12. Levi: Arb. a. d. Neurol. Instit. Wien. Univ., 1917, II, 28.
13. MacWilliam: Brit. M. J., 1901, II, 1595.
14. Piper: Electrophysiologie menschlicher Muskeln, Berlin, 1912.
15. Salomonson: Folia Neurobiol., 1910, IV, 1.
16. Snyder: Am. J. of Physiol., 1913, XXXII, 329.
17. Snyder: Am. J. of Physiol., 1910, XXVI, 474.
18. Tileston: Am. J. Med. Sci., 1913, CXLVI, 1.
19. Williams: Am. J. of Physiol., 1916, XL, 230.

DESCRIPTION OF PLATE

FIG. 2.—Ankle clonus; electromyogram from gastrocnemius muscle. (See Table II, Film 2.)

FIG. 3.—Patellar clonus; from rectus femoris muscle. (See Table VIII, Film 9.)

FIG. 4.—Patellar clonus ending in spasm, electromyogram showing the transition from periodic to tetanic waves. (See Table IX, Film 5.)

FIG. 5.—Patellar clonus, low speed film, showing that the periods are longer at the beginning, and quickly shorten to a more constant periodicity, in this case the periods are: .17, .14, .12". (See Table VIII, Film 4.)

FIG. 6.—Patellar reflex, showing single diphasic wave.

FIG. 7.—Patellar clonus, record taken immediately after Fig. 6 without shifting electrodes. Clonus set up by steady pressure on patella. Note that each contraction has several action-currents.

In each case the upper tracing is the shadow of the tuning-fork vibrating at 50 D. V. per second, and the lower is the electromyogram.

# LAVOISIER AND THE HISTORY OF THE PHYSIOLOGY OF RESPIRATION AND METABOLISM. CONTEMPORARY VIEWS OF LIFE PROCESSES

By JOHN C. HEMMETER, M. D., PHIL. D.

Antoine Laurent Lavoisier, the son of a rich merchant, was born August 26, 1743, in Paris. Little can be ascertained concerning the degree of culture and the intellectual status of his parents. Alphonse de Candolle in his "History of Science and of Scientific Men" gives no reference to the genealogy. De Candolle, a member of the Academy of Sciences, Paris, would have been in a position to ascertain the truth on this point. Galton and Wilhelm Ostwald, who endeavored to trace the ancestry of Lavoisier. Prof. Edouard Grimoux (Lavoisier) gives the genealogy of this famous chemist on the paternal side back to 1620 (see Grimoux, pp. 325-331). There is no one in the list of ancestors from whom it could be claimed that Lavoisier received his great genius by hereditary transmission. The studies in the hereditary transmission of genius by Galton, de Candolle, Ostwald, and Raibmayr, find no family basis for their theories in the genealogy of Lavoisier. He was educated at the Collège Mazarin, his studies being directed towards the study of law. He soon developed a preference for natural science. He was instructed in astronomy by La Caille, in chemistry by Rouelle, and in botany by Bernard de Jussieu.

The earliest of Lavoisier's inquiries was an "Analysis of Gypsum," presented to the Academy of Sciences in 1765, and published in the collection of "Mémoires de Divers Savants," 1768. His next work of importance was a paper on "The Practical Illumination of the Streets of Paris," for which a prize had been offered by the Chief of Police, M. de Sartine. This prize was not awarded to Lavoisier, but his suggestions were of such importance that the King directed that a gold medal be bestowed upon the young author at the public sitting of the Academy in April, 1766. Two years later, at the age of 25, he was admitted to the French Academy of Sciences.

He sought and received appointment as "Fermier Général," a position unique in the French Government of that day. The closest approximation to it appears to be a sub-officer in the Department of Agriculture, controlling mainly the revenues (tax on salts, state sales on tobacco, etc.).

In this position he showed himself a skilful administrator. In 1776 Tourgot placed him at the head of the Régie des Salpêtres, where he introduced many improvements into the manufacture of gunpowder. From 1778 to 1785 he gave attention to agriculture and contributed many valuable suggestions to the science of husbandry. In 1787 he was elected to the Provincial Assembly of Orléans. In 1788 he became one of the trustees of the Bank of Discount and in 1789 he was an assistant deputy to the Constituent Assembly. In 1790 he was a member of the Commission on Weights and Measures and developed great interest in the preparation of a new decimal system. In 1791, as one of the commissioners of the Treasury, he published an essay "De la Richesse Nationale de France," in which he presented a plan for the collection of taxes. It was said by the Minister of Public Instruction (who published all of his works from 1864 to 1893) that this essay was a forerunner of a complete treatise on this important subject, and entitles him to a high rank among political economists.

In the "Œuvres de Lavoisier," "*publiées par les Soins de son Excellence, le Ministre de l'Instruction Publique,*" 1864-1893, the incontrovertible evidence of great gift of exposition, power of logic and unparalleled acuteness is manifested. These works embody the principles out of which chemical science was to be renovated. His greatest work is his "Traité Elémentaire de Chimie," 2 vols., 1789, in which the basis of modern chemistry is laid. In 1777 he published in the "Memoirs of the Academy of Sciences" an essay, "Du Principe Constitutif de la Chaleur," which marks the transition of his attention to the application of chemistry to physiology. Some of the more specific experimentations on physiologic chemistry will be explained at a later stage. By this time, the revolutionary movement against Louis XVI and

ANTOINE LAURENT LAVOISIER. BORN AUGUST 26, 1743. EXECUTED DURING THE FRENCH REVOLUTION, MAY 8, 1794.

Marie Antoinette was in full progress. He was collecting all his writings with the ultimate view of remodelling them into a single work, when the course of the revolutionary events brought him to a premature end. Dupin, a member of the Convention, having on May 2, 1794, introduced a formal accusation against all the farmers of the public revenue (Fermier Général) Lavoisier delivered himself up and was imprisoned. On the 6th he was involved in the general sentence of death against the corporation to which he belonged, and two days later he was guillotined. His essays were collected and published by his widow (who afterward married Count Rumford), under the title of "Mémoires de Physique de et Chimie," in two volumes. A complete edition of his works has been published under the supervision of the Minister of Instruction at the expense of the government (4 vols., Paris, 1864-1868).

*Literature.*—Grimaux: "Lavoisier, d'après sa correspondance, ses manuscrits, ses papiers de famille et d'autres documents, inédits (1888)."

Schultze: "Lavoisier der Begründer der Chemie."

Gunning, J. W.: "L'Empirisme et la Science. Esquisse Historique sur Lavoisier. Archive neederland. de sc. exactes, etc. La Haye, 1871, VI, 473-483."

For Portrait, see "Hundred (The) Greatest Men," Vol. 6, London, 1880. Also Purland, T.: Collection II.

Brougham (Henry, Lord Brougham): "Lives of Philosophers," see chapter on Lavoisier.

During the years which followed her husband's death, Mme. Lavoisier was preoccupied with numerous affairs of a personal nature. These finished, she hastened to complete the task undertaken by her husband and arrested by his death.

In 1792 Lavoisier had conceived the idea of publishing his principal data, and of collecting the works of the other scientists who had contributed to the making of modern chemistry a greater science. This work was to be compiled in eight volumes. The first imprint was made at the end of April, 1793. Lavoisier, with the help of Seguin, did the proof-reading during his detention. When he died, the first two volumes were almost entirely printed, as well as a few pages of the fourth. The fourth year (1796), Mme. Lavoisier had a meeting with Seguin in order that these works might appear before the public and asked him to edit a preface, but she required that it should brand the men guilty of Lavoisier's death. Seguin refused. "To denounce those who had him condemned or who let him perish does not strike my fancy and, on the other hand, would diminish the horror that the event has left in all hearts. There are certain things more difficult to tell than to have told by the consciences of those to whom they were presented. Oftentimes they acquire more force from these witnesses. If you do not agree with me, you may have your own views printed; in your own words they would acquire a more convincing tone, proceeding directly from you." (Letter from Seguin dated July 18, 1796.) At the same time, he sent with this letter a sample of a preface which could never have pleased Mme. Lavoisier, for he attributed to himself an equal part with Lavoisier in the project of the publication of the works, saying, for example, "The plan *we* had thought about, the design *we* were meditating," etc.

Mme. Lavoisier gave up the project temporarily but took it up a few years later. She edited an introduction herself, in which she explained the conditions under which Lavoisier had undertaken this work. We publish it in its entirety:

**In 1792, Lavoisier conceived the idea of making a collection of all his works that had been read at the Academy during the 20 preceding years. In a way, it was the making of modern chemical history.**

**To make this history more interesting and more complete, he had proposed to add the works of those who, having adopted his system, had made experiments in his behalf.**

**This collection was to number about eight volumes.**

**Europe knows why they were never completed.**

**Almost all of the first, all of the second, a few pages of the fourth, have been finished.**

**Many scientists have desired to see those published. We hesitated a long time. It is difficult not to feel a certain fear when it comes to publishing the unfinished works of a man who justly enjoys a great reputation. It is when we have lost him that friendship must become impartial and show only what might add to the glory of a cherished and honored name.**

**We would have persisted; and their fragments would never have appeared if they had not contained (page 78 of the second volume) one of Lavoisier's ideas which claims, from the accompanying proofs, that he was the founder of the new chemical theory.**

**Thus it becomes a duty to confirm the views which scientists have expressed in regard to this question.**

**We beg their indulgence for the mistakes that may have been made in some other part of this collection.**

**They will surely grant this request when they learn that most of the proofs were reviewed in the author's last moments, and that, although he did not ignore the fact that his murder was premeditated, M. Lavoisier, calm and courageous, compiling a work which he thought would be useful to science, gave a memorable example of the serenity which intellectual purity and virtue can produce in the most unfortunate hours.**

The two volumes of the "Treatise on Chemistry," published in 1805, were not placed on sale, but given to all of the eminent men of this period. Cuvier thanked Mme. Lavoisier in the following words for her gift of the work to the class in sciences at the Institute:

**Madame, the class requests me to thank you for the work which you have so kindly given them, precious to all as well as to each one. Allow me to offer the testimony of my gratitude. All the friends of science are indebted to you for your heroic determination to publish this collection, and to publish it as it had been originally planned, a sad memorial of your loss as well as theirs. These incomplete volumes, these unfinished utterances, make a profound impression. What truth, it seems, we were about to learn in a book which began with so many truths so beautiful and so new, and yet how we feel the horror of the crime renewed in all its force, a crime which has afflicted humanity perhaps for centuries!**

Historical comments upon scientific researches are subject to manifold errors. The language of science has undergone so many changes in the course of time, that it is often difficult to grasp the real ideas of an author, even though he writes in our own mother tongue. The more distant his views may be from ours, the more readily are we tempted to form erroneous impressions of his meaning. Indefinite announcements often have been considered as discoveries, which were actually and really only made at a later period. Deficiency of exact scien-

tific knowledge occasionally produces erroneous ideas, which may engraft themselves as truths, by repetition; whereas, if such false ideas were not permitted to take hold of us, our thoughts would be led in another, safer and surer, direction.

No one can become independent of the influence which intellectual activity exerts upon seemingly wholly different fields of contemporary knowledge. Sensational discoveries are at once applied to other branches of science, and like newly issued coins, no matter how limited in value, are overestimated, until further investigation reveals their inferiority.

All this is true of our own time, and if this is so, we may conclude that much which is regarded as genuine coin to-day will be cast aside as spurious by those who come after us. We have a right to hope, however, that as methods of investigation improve and the true value of the acquisition of knowledge increases, there will be less need for elimination in the future. It is precisely to this matter of advance in the methods of experimentation that I wish to call your attention.

I will not take you back into remote times, only a period of 123 years, and review the ideas which engaged the minds of men of that time on the remarkable phenomena of nature. The great question of the difference between the organic and the inorganic world has from ages immemorial been uppermost in the mind of the scientist.

The status of the natural sciences about the middle of the 18th century was by no means a low one. Bacon in a most exemplary manner had defined the fundamental principles of inductive research; and eminent investigators, such as Galileo, Kepler and Newton, by observation and experiment, had established the most important fundamental laws of physics. In the science of man, the advances in anatomy by Vesalius were enhanced by the discovery of the circulation of the blood by Wm. Harvey, and placed upon a firm basis by the work of Haller. Chemistry enjoyed special growth about this time and we shall consider this with greater detail since the activity of Lavoisier is most intimately associated with its development.

In my biography of Haller (Johns Hopkins Hospital Bulletin, Vol. XIX, March, 1908) I referred occasionally to one who stood at the head of science of that epoch—Geo. Ernst Stahl—one of the foremost minds of his time, whose views not only controlled chemistry, but general medicine as well. Stahl's influence rested upon the fact that he understood how to gather together into one general viewpoint the various natural sciences of his time. We may at this day reject as false his so-called "phlogiston" and "anima" theories, but we must not forget that both had a great value, because the sum total of the then existing knowledge was embraced in a unity in Stahl's doctrines which thereby accomplished what we now expect from each single theory.

When Lavoisier began his career, the phlogiston theory was universally recognized and he too was fully in accord with it, for he included the hypothetical heat substance and light substance in his table of chemical elements. (See Wilhelm Ostwald: "Die Forderung des Tages," p. 18.) Looking upon his researches from their beginning, we can trace, step by step, the method by which he at first hesitatingly, then with ever-increasing certainty, began to doubt, and with convincing passion for new truths, began to criticize and finally demonstrate the untenableness of the hypotheses of Stahl.

Lavoisier did not bring about this advance by his own exclusive efforts, but by the adroit use of the discoveries of his contemporaries. He is, however, clearly entitled to the honor of having originally applied the measures adopted at a later time in chemical processes and by which he really is to be looked upon as the founder of modern chemistry. Borutteau in Neuberger and Pagel's "Handbuch der Geschichte d. Medizin" calls him the *"Vater der modernen Chemie."*

It is not my intention to review in general all the work of this great man. His achievements proper have been detailed sufficiently often, and for lack of proper time I must refer you to the excellent statements of Grimaux, Neuberger and Pagel (*l. c.*), Kopp, Ladenburg, E. V. Meyer, Würtz, Lord Brougham, and others. One more point I wish to dwell upon, namely: Lavoisier's demonstration of *the established fact that in chemical processes the amount of matter present is neither increased nor diminished. This fact, first demonstrated by him in a number of experiments, has since become an established law, the law of immutability of the matter present.* This law applies not only to processes pertaining to inorganic, but also to organic substances and for all interchanges between these and the outside world. Clear as this is to us now, many statements appeared in the text-books during that century contradicting these theories. According to Vauquelin, for example, calcium is generated in the body of the chicken, because he thought he had discovered that more of this substance was excreted than had been ingested by this animal.

The prominent position which Lavoisier holds in the history of physiology is due to his series of researches in special physiologic chemistry, overthrowing the then existing *"vitalism"* of Stahl as in his chemic investigations he destroyed the *"phlogiston"* doctrine.

The subject of fire and heat has attracted the attention of naturalists from time immemorial. Stahl (1660-1734) explained these phenomena by affirming that "heat matter" was contained in all combustible bodies and was made to appear when such bodies were burned. He called this heat matter *"phlogiston."* Lavoisier, however, showed that the burning of combustible substances—coal for example—depended upon the oxygen contained in the air, an element recently discovered by Priestley (1774) and almost simultaneously by Scheele (1775); also that animal respiration is a process of combustion by which this O combines with the other bodily constituents of the animal, and that by this union with O the expired air contains $CO_2$ and $H_2O$, as already previously demonstrated by Black. True to his theories, and not satisfied with his general proofs of these processes, he and Seguin made numerous examinations of the expiratory air of man and animals, and thus added largely to the furtherance of our knowledge of the phenomena of life. Since then his experiments have often been repeated by almost identical methods.

When we consider that Lavoisier was the originator of the practical methods, even of elementary organic analyses in use at the present time, and that by the same he demonstrated the composition of the organic substance as made up of C, H, O,

and the occasional presence of N, we can realize that he laid the foundation of physiological chemistry in such completeness that his successors could merely build upon the structure he had created, but for many years could not contribute any material additions. We have, however, not exhausted the subject of the value of Lavoisier's discoveries. A far greater contribution will have to be considered—the explanation of *animal heat.*

Physiologists of all times have endeavored to expound the phenomena that certain members of the animal world, all mammals and birds, during life, possess a temperature far exceeding that of their surrounding conditions, and unchangeable under the most diverse circumstances. Some assumed that this body heat is inborn in the animal, with about as much reason as that of the animists, who held that it was a product of the soul or of the *life-spirit,* to which all the mysterious problems of life were attributed. An exception to this was made by the so-called iatro-mathematicians, who accounted for body heat by the friction of the blood circulating in the vessels, or compared it to heat generated during putrefaction and fermentation, which may have come near enough to truth without leading to further conclusions, as no one understood the cause of heat formation in those conditions. After Lavoisier, however, correctly interpreted the process of combustion and recognized the similarity of the physiologic chemistry of respiration to combustion, he was naturally led to view the heat formation of animals from the same standpoint.

The adherents of the phlogiston theory looked upon fire or heat as a matter, or element, like their other "elements"—earth, water and air. During combustion and the so-called "calcination" of the metals, "phlogiston" and with it heat was liberated from the burning bodies. Later when combustible H gas was discovered by Cavendish in 1781, many claimed that this was phlogiston proper, or air highly charged with it; whilst, on the other hand, O was thought to be "dephlogisticated" air. These views took such a firm hold on the chemists of that time, that even the well-known fact of increase in weight during calcination, which Lavoisier showed to be due to absorption of O, did not convince them to the contrary, but they rather added a new hypothesis, namely, that phlogiston possessed a "negative weight." $CO_2$ was discovered by Black in 1757. N by Rutherford in 1772. O by Priestley, 1774; Scheele, 1775; Lavoisier, 1775; Hirn, 1781.

When, however, Lavoisier had become thoroughly convinced of the untenability of the phlogiston theory, he could not but draw into his investigations the heat that was generated during all processes of combustion. Like other naturalists he still supposed this heat was some form of matter, although unweighable; an imponderable substance, such as magnetism, electricity and the like. Although this conception has been given up, the method of estimating heat, first demonstrated by Laplace and later utilized by Lavoisier to measure the heat produced by animals, still holds good to-day. And since they compared the heat given off with the expired $CO_2$ they believed from their experiments that animal heat was a result of combustion going on in the body.

For the first time a firm foundation was laid for the understanding of the fundamental phenomena of animal life. The conceptions of the times were like this: The animal body is in the main composed of matter consisting of C, H, O and N. These elements may, however, take up a larger amount of O than they originally contain; therefore, they unite with the O transmitted by respiration whereby $CO_2$, $H_2O$ and certain nitrogenous bodies are formed and are expelled. By this combustion, heat is generated. Now since a portion of the body substance is removed by excretion, the animal loses in weight. This loss is replenished by the food substances, which are composed of the same elements as the animal body itself, so that with proper intake it will continue its existence for a longer period of time. Life process, in many respects, may be likened to the burning of a lamp; in fact, the materials fed to the latter are identical in composition with the food-stuffs.

These are the principal features of the theories advanced by Lavoisier as a result of his physiological investigation, of such striking simplicity and so amply verified by experiments, one would think that the physiologists of his time would eagerly seize them in order to emerge from the difficulties of understanding the phenomena of life. This was by no means the case, and by study of the literature of that period, we shall endeavor to ascertain the reasons therefor.

Although the reign of the phlogiston theory fell by the blows given by the chemical discoveries of Lavoisier, and all reputable chemists sided with the antiphlogistic theory (as it was then termed in contradiction), still neither physiologists nor philosophers, and least of all the chemists, in reflecting upon the phenomena of life, could rid themselves of the opinion that these phenomena were of an entirely different order from those of inorganic nature, and, although similar in character in some details, must arise from some special power or cause of their own. Lavoisier's chemical theory of respiration and heat production gave no answer to the difficult question what life really is, and no satisfactory answer to the question, what the hypothetic cause of animal heat was, whether, according to the hypothesis of Paracelsus, it might be called *archeus,* or, according to Stahl, it was the *anima,* the soul or vital force. The thinkers of the time inclined to the same views upon which the alchemists based their theories. Like those who searched for a matter, the *"quinta essentia,"* which should convert all metals into gold, the possessor of which would become wise and immortal, so did these investigators search for a term or formula by which all enigmas would be solved and all secrets disclosed. And since no such formula was discovered, shorter terms, at least, were adopted for the restricted field of phenomena. As to the phenomena of life in particular, some attributed them to vital force itself, others to the *"nisus formativus"* of Blumenbach, and yet others to the "irritability" theory of Haller. The most generally adopted view was that of Stahl, who looked upon the characteristic of life substance as the power of resistance against putrefaction.*

* "Vita nihil aliud est formaliter, quam conservatio corporis in mixtione quadam corruptibili, sed sine omni corruptionis actualis eventu."

In the fortifying and dissemination of these views much was done by a man whose achievements in other fields of scientific labor deserve our fullest recognition, Xavier Bichat. He is the creator of general anatomy, from which our present histology or the finer study of the tissues became developed. As a true adherent to the *vitalistic* school, chiefly upheld by the University of Montpelier, he extensively spread this study in his works and for a long time held unlimited sway. His definition of life, "La vie est l'ensemble des fonctions qui résistent à la mort" ("Life consists in the main of the functions which resist death"), is fundamentally nothing but a transcription of Stahl's theory. Bichat's great influence, especially in his own country, is to be attributed to his elegant and attractive manner of discourse, rather than to the inherent value of his teachings.

According to Bichat, we have to distinguish between two kinds of bodies, animate and inanimate, and two series of phenomena, physical and physiological. The first are produced by physical causes, weight, electricity, etc., the other by physiological, the capacity for extension, contractibility and irritability. The first act according to unchangeable laws, the latter do not. It is therefore impossible to determine the physiological phenomena by the same methods of physical investigation, and he speaks with some contempt of these efforts, clearly alluding to Lavoisier, without, however, mentioning his name.

To this inward impulse for knowledge and the search for an uppermost principle, two especial contemporaneous products of thought came to aid, which again are closely interwoven, *natural philosophy* and *galvanism*. Natural philosophy, in the form given to it by Schelling (system of 1797), had exerted the greatest influence in the development of the natural sciences, especially in Germany. This influence has been much dwelt upon and has met with severe condemnation, which its later excrescences justly deserved. A complete estimate of natural philosophy as conceived by Schelling cannot here be undertaken and only the effects of these theories on the conception of the process of life will be pointed out. Schelling places the highest law of nature upon a trinity: everything springs from two opposite activities, united together by a third—(I) the expanding, (II) the retarding activity and (III) the weight—which are to be looked upon as the equivalent of matter, whereas the latter represents the product of the three activities. Nature as a product of the active substance proper is represented as inorganic, organic and cosmic. The activity of nature is retarded in the first, productivity is continued in the second, whilst in the cosmic the co-existence of the first two is brought about. In *inorganic* nature, the trinity is exhibited as magnetism, electricity and chemism; in the *organic*, as sensibility, irritability and reproduction; in the cosmos, as light, weight (gravitation) and accelerating and retarding force. All organization proceeds from light, which corresponds to world soul, and tends to the production of intelligence. This, however, is attained only in man, the *microcosm*, who also encompasses everything contained in the *macrocosm*, and therefore can produce everything in the form of thought. The laws of nature must therefore be regulated by the laws of consciousness, and the one may be deduced from the other. See Schelling's view of nature in "History of European Thought in the 19th Century," by John Theodore Merz, Vol. III, p. 556, etc.

The broad and sympathetic interpretation of John T. Merz can make even the obscure speculations of Schelling appear interesting to a modern physiologist.

In this system, of which no adequate conception can be made from these preceding sentences, analogies play an important rôle. They must often take the place of proof. The influence of galvanism with its polarities is unmistakable. This very fact induced physiologists of that time to take sides with that system. Galvani's discovery of the wonderful effects of the constant current upon muscles and nerves had made a powerful impression. In galvanism the key was sought and found for the phenomena in nerve and muscle activity and later that of life phenomena. Thus, for example, Prochaska, the Viennese physiologist, in the preface to the renewed edition of his text-book in 1820, states that *"life processes and galvanism rest on the same foundations,"* and boasts that the new edition was worked according to this principle, as is seen from the title on page 47 of the chapter on this subject, *"Life as a matter of fact proceeds from the laws of electrical processes"* The number of treatises on the subject of galvanism which appeared at that time is too great to enumerate. I will mention only one, because it is interesting on account of its author—Alex. v. Humboldt's work in two volumes, on irritability of muscle and nerve fiber.

Looking over the text-books of that time, we find everywhere traces of these influences and I shall refer to one in particular because it is typical. Geo. Friedr. Hildebrandt, professor of physics and chemistry at Erlangen, is best known by his text-book on anatomy, which appeared in 1789-1792, and was revised in 1830-1832 by E. H. Weber, the same who discovered the inhibitory action of the vagus on the heart in 1845. He is also the author of text-books on chemistry and natural sciences, and his work on physiology, first published in 1796, was republished by his son-in-law, Hohnbaum, in its sixth edition, from manuscripts he had left at the time of his death. Hildebrandt was a sober, industrious worker with astonishingly broad knowledge. He constantly emphasized the importance of experience as against construction from general and convincing hypotheses. In spite of this, especially in his later edition, "polar matter" and "*Grundkräfte*" ("fundamental forces") play an important rôle with him. All matter is grounded on the union of the dual expansible and attractive force. These may also become disassociated, in which case the superfluous will act also upon distant bodies. By this are generated magnetism, electricity, chemical processes and the higher stage, life. For this reason both forces act during life; the *expansible* more so, which appears as light in its free state, but in the living body as *life-turgor* (I gather the impression from Hildebrandt's book that he uses the word *turgor*—from turgescere, to swell—as modern physiologists use the word "tonus" or tonicity) by which development and growth are

brought about. The *attractive* force, however, is not missing, for from it we have the chemical and mechanical processes.

All this may impress one as a play of words. The same is felt by the author, for he continues immediately after his exposition, as follows: "However, we must not conclude after these explanations that we have lifted the veil of the secret of life, which covers that of the entire creation. All is hypothesis that our physiologists have to offer as to the problem of life, and what the older physiologists said about the same, although more recent investigations have penetrated deeper into the mysteries of nature than was possible with the former." The "deeper penetration" refers to Schelling's natural philosophy and as pictured in the mind of Hildebrandt. However, on the whole, he was not inclined to be speculative and had he appeared in the middle of the 19th century, he would have been looked upon as a rank "materialist."

According to him, nature yields only matter, coarse and fine; by the latter he means imponderable, and it has been so designated from that time to the present. By admixture only of these, all phenomena are, and even life is, produced, not as Reil thought by mixture and form, because the latter is contained in the former, being generated by it.

Reil plays the same rôle for vitalism in Germany as Bichat does in France. He founded the "Archives for Physiology," the first volume appearing in 1796 and containing an extensive treatise on the life energy—"Lebenskraft." According to Reil, there are two series of phenomena: (1) Matter and (2) conceptions (opinions). The phenomena of the living body, in so far as they are not due to the conceptions or opinions, have their foundation in animal matter, in the mixture of matter (admixture) and form, that is, chemical combination. He holds that "energy" is the relation of these phenomena to the properties of matter by which they are generated; consequently, "vital energy" results from material circumstances, but is not perceptible to the senses owing to the incomplete state of chemistry and lack of knowledge as to the nature of the so-called "imponderables." Therefore, every organ, every tissue, possesses its own vital power due to its chemic composition and form. In his endeavor more closely to confirm these properties, Reil then also resorts to defining life phenomena as "potential galvanic processes."

The unfruitfulness of all these speculations, especially their outgrowths, which natural philosophy of that period carried on, was that no special research for facts was made in single and individual problems or fields of research, but the thinkers aimed to trace everything from the "uppermost principle" by deduction and intuition. This was the reason for naturalists of better mind entirely to turn away from these theories. In justice, however, we must admit that philosophic ideals had a stimulating effect on many branches of our sciences, especially embryology and comparative anatomy. The fundamental phenomena of animal life, however—namely, Lavoisier's discovery of continuous oxidation of its component parts, and the metabolism accompanying it—remained unsolved. Even such an erudite man as Herman Lotze, physician and philosopher, could not arrive at a clear understanding, and as late as 1851, in his "General Physiology," he makes an unsuccessful attempt to explain it teleologically, by the assumption that the body by its continual changes in its component parts is rendered more able to resist outside disturbance. Likewise, the eminent Johannes Müller, who embraced so masterfully the entire physiologic knowledge as it was understood up to his time, could not arrive at a correct conception regarding this fundamental question.

Lotze was one of the first scientifically to attack vitalism, without, however, making much impression. He strove to justify the teleological viewpoint in a philosophical way. It appears possible that this viewpoint can be directly deduced from the premises of the old natural philosophy, but his arguments are defective. As a fact, there undoubtedly is a definite conformity to purpose and to arrangement in organic nature; however, it is not restricted to organic nature, but belongs to nature in its entirety, and to understand the details it is often necessary to ask what purpose or object is fulfilled by this or that part of the whole organization. We must, however, be very careful not to overlook the fact that we are introducing a conception thereby, which can have a meaning only from the standpoint of an individual who acts with a precise and conscious purpose; objects of nature, however, present themselves to our investigation as concrete objects. It is not necessary further to expound to this audience Darwin's theory as to how living things develop conformably to purpose.

Chemists are justified in feeling an inspiring pride in the contributions their historic fellow-workers have made to physiology, for the next impetus to revivifying physiology came from J. Liebig.

After having materially improved upon the elementary organic analysis created by Lavoisier, he applied his vast knowledge of chemistry to the study of conditions of nutrition in animals and plants. What he taught in this field is in part less the result of experimental investigation than it is deductive conclusion from basic chemic principles. Much of this has been found to be erroneous. Nevertheless, he is entitled to the credit of having spurred on the scientific investigation of metabolism and to have again pointed out to physiologists the important significance of Lavoisier's fundamental doctrines.

Before proceeding further, we must go back to the end of the 18th century and consider the life process in plants, especially their nutrition. As early as 1779, Priestley discovered that plants were capable of converting the atmosphere of confined spaces, which had proven fatal to animals, in such a way that the air again became respirable. In the same year Ingen-Housz showed that only the green parts of the plant were capable of doing this, and then only in the light, that they absorb $CO_2$ and exhale O, that contrariwise in the dark all plants, and those not of green color always, take up O and give off $CO_2$ just like animals. In the further course of this research he established his theory of plant nutrition. He showed that the carbon which the plant stores up during its growth could not come from the soil, but from the carbonic acid of the atmosphere, the oxygen of which is liberated whilst the carbon combines with the elements contained in the water

(and in part with N) taken up by the roots. His discoveries were in the main confirmed by Senebier, who, however, erroneously supposed that carbonic acid was absorbed by the roots. Th. de Saussure studied these processes more accurately and demonstrated that larger amounts of $CO_2$ act favorably upon the plant only in strong light (atmospheric air contains but a small quantity of $CO_2$, only 3 to 4 parts in 10,000); that the increase in the weight of the plant is greater than the amount of carbon taken up, because water and salts, the latter in slight quantity only, are absorbed from the soil; that respiration goes alongside with the decomposition of $CO_2$ even in the light; that the plant does not absorb N from the air but from the soil, which was later positively confirmed by Boussingault. If we add to this that Maret in 1834 showed that fungi, which lacking in green coloring matter (chlorophyl) take up O and give off $CO_2$, we shall have summarized what Liebig found already established when he entered the field of investigation of plant nutrition.

In spite of these achievements the practical agriculturists, as well as the theorists, clung to the theory that the so-called "*humus*" was necessary for plant development and that the plant derived its whole sustenance and carbon from it. Liebig had completely set aside this "*humus*" (soil) theory and thereby gave to agriculture a rational principle of fertilizing. For us it is of greater importance firmly to settle the so-called circulation of matter in the organic nature. The plant takes $CO_2$ from the air, N and $H_2O$ from the soil and forms organic bodies from these substances, which with the addition of a small amount of salts make up the greater portion of the plant. Plants serve as a nourishment to animals, directly to herbivora and indirectly to such carnivora as thrive upon herbivora. In these the C is in part again converted into $CO_2$, and H into $H_2O$, whilst another portion of these bodies is excreted in combination with N, in a form which in turn readily passes over into $NH_4$ and as such is again taken up by the plant. The same products result from putrefaction in both animal and vegetable bodies. Therefore, the fundamental law of *conservation of matter* discovered by Lavoisier on a small scale for chemical processes has been shown to take place identically in the larger interchanges of matter transformations throughout the earth.

In spite of the emphasizing of the chemical standpoint in the consideration of life phenomena, Liebig held that these depended upon a special vital power, which, however, did not set aside chemical influences, but directed the same and held them in check. This general view held by all writers of that time may be traced back to the apparent difficulty in understanding how the living body maintains its composition, whereas immediately after death it becomes dissociated by decomposition or putrefaction. In reality this difficulty does not exist, since the living body is constantly being attacked and partially consumed, with this difference, that during life the substances lost are at once replaced.

Whilst up to this time the chemical view was exclusively held with regard to these discoveries, physical views came to the foreground in the middle of the last century, incited by Helmholtz through his epoch-making publication, "On the Conservation of Energy." From this viewpoint du Bois-Reymond in his celebrated introduction to his "Researches on Animal Electricity" explained the untenability of the doctrine of the *vital force* and emphasized particularly that the phenomena of life cannot be differentiated from the inorganic world and that it is the province of science to make plain both series of phenomena upon identical principles in so far as it is scientifically possible.

We have seen above in what manner Laplace and Lavoisier attempted to explain that animal heat was slowly produced by slow combustion going on within the body. But their experiments and calculations were not exact enough to settle such an important question. Dulong and Despretz in 1822 sought to determine the matter by new experiments urged on by the prize offered by the Academy of Paris. They arrived at very incomplete results, for according to Dulong only 75 per cent and Despretz 80 per cent of animal heat is generated by combustion. How the balance of 20 and 25 per cent was produced remained a complete mystery. So that it is not to be wondered at, that in the many writings on physiology it was always suggested to that animal heat was something especial, that it was caused by the nervous system, or by vital force, and that, therefore, no constant relationship was necessary between the heat produced and that of the material burned.

Still later, it was shown that neither the experiments of Dulong nor of Despretz nor their methods of calculations offer a binding conclusion and that we have sufficiently concordant estimations in the results of experiments and calculations of caloric values of the nourishment taken, provided we extend the experiments over longer periods and make sure that the animals remain in equilibrium of nitrogen and carbon; *i. e.*, to be in a condition in which an amount of material will be actually oxidized in the organism that is equivalent to the food taken in. This question again depends, as we shall see, upon the law of the "conservation of energy" or as some preferred to call it, "the immutability of stored up energy." By energy we understand the ability to perform work. Daily experience teaches us that the particles of matter attain this ability when they are in motion. A leaden bullet held in the hand is a most innocent object, but when great velocity is imparted to it by the pressure from the gases of the explosion of powder in a gun, it will shatter bone and penetrate steel. Principles of mechanics teach that the energy thus produced can be measured by the work rendered and estimated as one-half of the product of the mass by the square of its velocity. What pertains to the leaden ball holds good for every other substance.

Imagine now two stones of equal weight, one lying on the ground, the other on the roof of a house, and that the latter by some cause is pushed over the edge of the roof. In falling it acquires an increasing rapidity according to Galileo's law. Upon striking the ground it can produce a certain effect or work which the other stone cannot. We see then, that besides *energy of motion*, there is another *energy of position*. The latter differs mainly from the former in that it becomes capable of giving off work when it passes over to energy of motion. It

has been therefore called *latent* or *potential energy* (older term was *elasticity*), whilst the first was termed *living* or *kinetic energy*.

Numerous experiments have demonstrated that energy of position (potential) is true not only for the mass forms of energy, but also for the smallest particles or molecules that go to make up the mass. This is known as chemical combination, but during this process there is a transformation from potential to kinetic energy—comparable to the transformation from the energy of position (potential) of a stone resting on a high place, and the same stone started on a fall downward toward the earth (energy of motion or kinetic energy). By the union of H and O molecules heat is formed, which is assumed to be due to change in the relative positions of H and O atoms. The amount of heat thus generated can be measured by appropriate instruments, just as the heat produced by the impact of a falling object has been measured. The molecules acting in a body seemingly at rest are assumed to be in continual movement, and the energy produced by this inward motion when exerted upon our nerves we designate heat. Now this form of energy may be transformed to the visible motion of masses or reversed, and here again the rule holds that the supply of energy is neither increased nor diminished. Finally, the same rule applies to all known forms of energy, electricity, light, chemical action, etc.

Single portions of this important law of nature were long known to physicists, but the general interpretation was first recognized, though perhaps defined in a vague manner, by the physician, Julius Robert Mayer, of Heilbronn. Helmholtz independently recognized the same law and gave to it a definite mathematic expression, summing up all actual proofs gathered up to that time. These have since then multiplied greatly, but not a single experience is found to contradict this law. We have to conclude then, that there is a supreme law of conservation of energy which substantially supplements the older law of the *immutability of matter*.

To explain the importance of this law for the better understanding of vital phenomena, I must add a word regarding the connection between heat and chemical processes. When in a mixture of H and O the molecules of these gases are set in motion with more or less rapidity, according to the temperature, the median distance between the molecules of these gases remains unchanged. If we apply a flame or electric spark to the mass, a mutual interchange takes place, H and O disappear and we have $H_2O$ instead, in which the H and O unite to form a new combination composed of the same molecules. This is known as a chemical union and may be likened to the process of the falling stone. Like this, the reciprocal position of stone and earth, in the latter the particles of H and O are changed, only that through this change heat is generated, a process that can be measured and estimated by means of the calorimeter. The potential energy (energy of the *position* of older writers) *of the H and O particles* is therefore converted into kinetic energy in the form of molecular motion which we call heat.

Many experiments have shown that in this union of the same quantities of H and O, one and the same amount of energy is involved in the form of heat. One kg. of H oxidized into $H_2O$ produces an amount of heat that will raise 34,000 kg. of water from 0° to 1° C. This is known as the combustion heat of H and we may likewise so designate the combustion heat of C or that generated by any other chemical combination.

Strictly speaking, these figures are not the true expression of combustion heat between H and O. Important reasons lead us to assume that the atoms, the smallest particles in H, are not present in a free state, but united or coupled by twos to form one molecule, the same being true of the atoms and molecules of O. Before union can take place between the atoms of H and O to form molecules of water, the molecules of oxygen and hydrogen must be separated. Since this requires a certain amount of energy, the final result of this combustion is a slightly smaller amount of heat.

The combustion heat is equal to the combination heat minus the so-called molecular latent heat.

This condition must be more fully considered when it concerns complex instead of simple bodies. For instance, the fats are a combination of C, H and O. They are capable of taking on more O and are combustible into $CO_2$ and $H_2O$. Lavoisier, as well as Dulong and Despretz, assumed that as much heat is generated as when equal quantities of free C and H are burned. As a matter of fact, however, the heat produced is smaller, due to the value of the latent heat in the atoms of C, H and O in the fat molecule. Just as heat is liberated by chemical union, we can analyze chemic compounds by heat. Red oxide of mercury is split into Hg and O on heating. The energy used up by this dissociation has always been found to be equal to the heat produced by combining the same elements in the same amounts. The law of conservation or immutabilty of energy applies here throughout.

After these lengthy digressions let us revert to the subject of living objects. Combustion goes on constantly in all animals. Substances containing C and H enter into them and free O is taken in with respiration, whilst both are given off in the form of $CO_2$ and $H_2O$. Heat is thereby generated in all animals, even in the so-called cold-blooded, which are usually not warmer than their environment, because they give up their body heat more readily. Plants also form heat from the O, combining with C and H. In many blossoms—for example, the *Aroides*—in germinating seed and in other similar substances, the formation of heat may be so great as to exceed that which is lost.

Animals not only produce heat, but also produce mechanical work. In a large measure, this is accomplished by the muscles. This act takes place through the energy of chemical combinations. It has been shown that the process of oxidation is actively increased in the working muscles. Working persons excrete more $CO_2$ than those who are inactive. The animal machine which we call muscle is in this respect exactly like a steam engine, a part of the free energy given off appearing in the form of free heat, only that the muscle works under more favorable conditions than the best steam engine. Whereas in the latter only about 10 per cent of chemical energy can be utilized for work, this proportion may under circumstances

reach 25 per cent in the muscle. Count Rumford claimed that a pound of hay given to a horse will yield far greater utilization effect than when the same is used for fuel in a steam engine.* (I have personal doubts as to the feasibility of such a comparative caloric test with the imperfect apparatus available in Rumford's days.)

The mechanical energy generated by combustion in the animal, when not used outwardly for work, is again converted into heat and therefore does not come into consideration in calorimetric investigations, where the animal is confined in a calorimeter. If, however, the experiment is conducted in such a way that some amount of the result is taken up in work, a correspondingly smaller portion of heat is set free, according to the above theory. Hirn, the physicist, has attempted experimentally to prove and estimate this mechanical heat equivalent from the relation between heat and work, but his experiments are not sufficiently exact to claim validity in comparison with the value of the heat equivalents obtained by other methods. In the United States Atwater and Benedict have solved this problem more successfully. For the modern physiology of this subject, see Howell, p. 963, sixth edition.

Animals obtain carbohydrates for nutriment from plants and give off the same in combination with O as $CO_2$. Plants take up this $CO_2$, split up the same and excrete it as O. Whilst energy is set free during the formation of $CO_2$, this must be utilized in the dissociation of the same. This energy is manifestly derived from the sun, since the splitting up of $CO_2$ can take place only in light. There is no doubt that the great heat of the sun represents an enormous storage of energy. A portion of this reaches the earth by radiation and so far as it concerns the green plants it is stored up in the manner described. This not only serves to sustain animal life, but must also serve to liberate heat energy when parts of plants or organic material are burned in stoves. With regard to coal and similar derivatives of plant life used for heating, it is well known that they are the result or effect of the sun's energy, which in part has reached this earth many thousand years ago. (See the "Origin and Evolution of Life" by Henry F. Osborne.)

All life then, animal and vegetable, comes from the sun. But whilst we may be justified in assuming a cycle of events, complete in itself for the organic world, we cannot explain the transformations of energy in the same manner. The energy given off in the form of heat by animals radiates into space in the same manner as the energy from the sun, which has served the purpose of heating the earth's surface. But animal heat thus radiated into space is returned to the sun in but infinitesimal proportions. If, therefore, there are no other special sources besides those of the sun by which we could replenish our supply of energy, and about which we know nothing, the day may presumably come when no more energy will reach the earth. Then all life will cease and the hour hand of eternity will have performed one revolution.

We have arrived at the goal of our travels. Whilst the path was rough and difficult, we have reached a height from which an extensive view over a vast and rich field is presented to us. This path has been largely planned and laid out by Lavoisier, so that but one, it is true the boldest, achievement was needed to reach the climax, and that was by keen research to confirm the law of the conservation of energy.

From this height it is impossible to consider details more accurately. If we step down and carefully examine the field of biological research, we shall recognize the fruits of the labors of so many workers. No opportunity is afforded to mention all. We should find everywhere many actively engaged in gathering in new fruits, sowing seed for future harvests or collecting crops preparatory for future cultivation. We should understand how the aid of chemistry, physics, and the astonishing advances in microscopical technics have cleared up the views of life processes. Above all things our attention would be drawn to a fact of which Lavoisier and his contemporaries had no inkling: the conception of the generation of living beings from elementary organisms or cells. This knowledge first begun by Schwann in 1839 has made tremendous progress. Histology and experimental physiology have continued the examinations of cell structure, as the laboratories of the finer processes of life.

However, let us rejoice in our present possession of truth which will serve as a starting point for new discoveries. Lavoisier's work has helped greatly to put us in possession of these basal truths. Chemists have long ago agreed that Lavoisier is the founder of modern chemistry. You will also admit from the foregoing that physiology also looks upon him as a pathfinder and owes him thanks for some of the most treasured acquisitions. But he also had predecessors who pointed out the way to proceed. As early as 1681, John Mayow recognized that only a portion of the atmospheric air was capable of sustaining respiration and combustion, and that this portion must be contained in saltpetre, for which reason he called it "spiritus," "fixed air." (See also article on Albrecht von Haller, section on respiration, by John C. Hemmeter in Johns Hopkins Hospital Bulletin, March, 1908.)

Going back still further, Leonardo da Vinci, a man of comprehensive and marvellous mind, who combined the genius of an artist with the talent of the scientist, recognized that fire consumed air and that animals could not live in the air which could not support the flame. We must also note that before Lavoisier, Priestley in 1774 produced pure O, and showed that it was absorbed by the blood and that dark blood was rendered bright red by it and that this absorption may also take place through the membranes, an important factor in understanding respiration. Lavoisier has been criticized by Lord Brougham for not being fair in acknowledging the claims of his predecessors. This may be possible, but one thing is certain, it was he who first established the doctrine of respiration and of formation of heat in animals and presented it in such form that all of his successors were enabled to add many single

* Count Rumford's real name was Benjamin Thompson. He was an American, born in Woburn, Mass., in 1753, and later on married Madame Lavoisier, the widow of the great French chemist of whom this article deals. (See Leading American Men of Science, edited by David Starr Jordan.)

details, it is true, but were not able to change the main fundamental principles.

*Addendum.*—As this article is intended more as a contribution to the history of biochemistry than a complete biography, I cannot go into the details of Lavoisier's unjust trial and execution, by the tribunal of the French Revolution in 1794. Lavoisier was guillotined with 21 others connected with the work of the *"Fermier Général."* After the execution the great Lagrange said to Delambre, *"Il ne leur a fallu qu'un moment pour fair tomber cette tête-et cent années ne suffiront pas pour en reproduine un semblable"* (Eloge de Langrange par Delambre Mémoires de l'Institut 1812 PXIV).

## BRIEF ABSTRACTS OF IMPORTANT PUBLICATIONS OF LAVOISIER

**Experiments on respiration in animals and the changes which take place in the air passing through the lungs. (1777.) Œuvres II, 174-183.**

Of all the phenomena of animal life none are more striking and none arouse the attention of the physicist and physiologist more than those which accompany respiration. Heated mercury absorbs about ⅙ its volume from the atmospheric air by calcination, the remaining air cannot sustain respiration and combustion. On heating the mercurial precipitate we obtain a gas, which when mixed with the rest of atmospheric air again resembles the latter. A sparrow when confined in an air mass of 31 cubic inches dies in 55 minutes; the volume of air is only slightly diminished, about 1/60. The residue cannot serve respiration or combustion and renders lime-water cloudy. Caustic potash decreases the volume ⅙, loses its alkalescence, effervesces with acids and crystallizes; briefly, it has become united to "fixed air." What remains after this absorption behaves just like the air in which Hg became calcined; if the respirable portion of ordinary air be now added we again have the latter. Therefore only two things are possible, either respiration changes the "respirable air" into "fixed air" (which Lavoisier calls *acide crayeux*, because it may be developed by treating chalk with acids) or an interchange takes place. [He inclined to the latter view because "respirable air" changes the blood to a red color like the metals (Hg, Pb, Fe) in calcination, but believes that both occur.]

**No. 4, p. 537. On the combination of "fire material" (*la matière du feu*) with vaporous fluids and the formation of aeriform elastic fluids. (1777.) Œuvres II, 212-224.**

An evidence of Lavoisier's inclination to the phlogiston theory. The author is of the opinion that there exists a very fine substance which he calls "matter of fire, of heat and of light" (*matière du feu, de la chaleur et de la lumière*) which permeates all bodies, forming with them an equivalent weight, not readily penetrable by each, and that this fluid exists in part free and in others (material bodies) in combination. The supposition is not new and its admissibility is proved by the conformity of the phenomena of which he treats and the fact that it explains all experiences of physics and chemistry. As with water with which a chemical combination is conducted, for example, in adding an alkali to an acid solution to form a neutral salt, a double rôle is played, in that a portion of the same enters into the combination, the other portion taking up the salt contained in the solution, keeping the particles of the salt apart, so that each part of the fluid contains an equal portion of the salt, so with "fire material" which permeates each body, a portion of which is in combination and the other free, keeping apart the particles of the body. In bringing together different substances, and chemical dissociation or union takes place, it depends upon whether or not the new formed substances require as much "fire material" as the original; in the latter case heat must either be set free, which is noticed in the result, or it is abstracted from the surrounding bodies. Since all bodies take up "fire matter," measurements of the same cannot be determined exactly. All vessels are also lined with pores through which "fire matter" passes in, so that it cannot be measured like a fluid or gas shut off. Cooling sets in upon evaporation, as shown by Richmann, Mairan, Cullen and Baumé, and vapors are therefore produced by the union of fluids with "fire matter." Descriptions of experiments which he made conjointly with Laplace on the evaporation of fluids under the cell of the air-pump and refutation of the claims of the heat given off from limestone and effervescing alkalies by addition of acids are also given.

**Mémoires sur la combustion en général. (1777.) Œuvres II, 225-233. No. 7, p. 538. Memoirs on heat (Lavoisier and Laplace, 1780). Œuvres II, 283-285.**

This work is in four parts. In the first the terms "free heat," "heat capacity" and "specific heat" are defined.

The authors do not decide between the two hypotheses on the nature of heat; according to one it is an imponderable fluid, whilst the other asserts that it is due to oscillation of the matter. They claim, what may be true of both views, the unchangeableness of free heat by simple mixture of the bodies, whereas in chemical processes it may be increased as well as diminished. At any rate we may formulate the rule that every change of heat, whether real or apparent, occurring in any alteration of the bodily system, must appear in inverted order when that body assumes its original state. They designate "heat unity" as the amount of heat necessary to raise 1 pound of water to 1° on the scale of 80°; they term "heat capacity" or "specific heat" the relative heat units required to raise equal masses of different substances to an equivalent number of degrees. Conditions may vary in different temperatures, but it may be inferred that it is sufficiently constant within the limits of 0° to 80°. Since the admixture method is not sufficient to determine the specific heat, they show how it may be measured by means of ice, and describe the theory of development of the ice calorimeter and the apparatus employed.

In the second part the value of specific heat is considered with reference to water for a number of substances; further, the heat which is generated by mixing $H_2SO_4$ and $H_2O$, Ca with $H_2O$, Ca with $KNO_3$, the combustion of various substances and the heat developed in a guinea-pig.

The third part consists of hypothetic considerations foreign to our subject.

In the fourth part heat from combustion of coal and the amount of $CO_2$ is again estimated and compared to that produced in a guinea-pig and the air expired. The comparison of value as to conformity is sufficient to warrant the conclusion that respiration is a form of slow combustion, and similar to the burning of coal. The heat generated by the lungs is taken up by the blood and distributed throughout the body, and, like Crawford, the authors believe that the difference of heat capacity between arterial and venous blood also contributes to this. From all this they hold that the maintenance of an equal temperature in animals, with constant loss going on, is in great part due to the generation of heat by the union of the inspired "pure air" with the bases of the "fixed air" furnished by the blood.

**Nos. 11 and 12, pp. 539 and 540. First memoir on respiration in animals. (1790.) Œuvres II, 688-703. Premier mémoire sur la respiration des animaux. First memoir on respiration in animals. (1790.) Œuvres II, 704-714. Premier mémoire sur la transpiration des animaux.**

These two works of Lavoisier and Seguin give a more exact description of their former experiments on respiration and animal

heat. In the experiments of Laplace and Lavoisier the amount of heat produced in animals was found to be somewhat greater than the $CO_2$ given off. The account for this L. (1785) gave his opinion that probably some H besides C was burned during respiration. Respiration goes on in pure O and in a mixture of O and N under various conditions precisely in the same manner as in atmospheric air. N is neither absorbed nor excreted, but can be replaced by other indifferent gases. The amount of O taken up is greater in a lower temperature and is increased during digestion and muscle activity. The bodily temperature changes but little in the latter, but the pulse is accelerated in almost direct proportion to the amount of work yielded, so that other exertions, not measurable, such as recitation, composition, etc., may be determined thereby in a mechanical way. The average amount of O used by a man in 24 hours is estimated as 2 lbs. 1 oz. 1 dr., the C excreted as 10 oz. 4 dr., and the H (calculated as indirect from the superabundant O) as 1 oz. 5 dr. 51 gr. The article closes with observations on the nourishment of the working classes, regulation of heat and disturbances of weight equivalents.

For the examination of cutaneous transpiration they used an air-tight covering for the entire body, respiration being conducted by means of a tube in mouth. They differentiate between pulmonary respiration and transpiration. They surmise that carbonaceous and hydrogenous fluid is transpired in the blood of the lungs and then burned. With the $CO_2$ and $H_2O$ thus formed the water is evaporated as excreted by the blood. The latter is lung transpiration water, the former lung respiration water. To estimate these separately, water is calculated from the O and C, with the proviso that all $CO_2$ originates in the lungs or the blood whilst circulating in the vessels. The sum total of respiration and transpiration is formed by weighing before and after the experiment, and the part taken by the lungs alone by weighing by means of the apparatus before and immediately at the end of the experiment, the difference then shows the part played by the skin. The authors are not deceived by the uncertainty of this hypothesis.

A résumé of all the published work by Lavoisier was given by Seguin alone in 1814.

# ABSTRACTS OF PAPERS

**Representing Work Done in The Johns Hopkins Hospital, but Published or to be Published Elsewhere than in the Bulletin Prepared by the Authors**

## THE INFLUENCE OF ACID PHOSPHATE UPON THE ELIMINATION OF AMMONIA IN THE URINE

W. McK. Marriott and John Howland

*(From the Department of Pediatrics, The Johns Hopkins University)*

In the course of nephritis, acidosis may develop, but the evidences of acidosis differ from those usually found, in that there is no increase in the ammonia of the urine. It would seem from this that the acid responsible for the disturbance of acid base equilibrium in nephritis is different in character from those causing acidosis in other conditions.

We have previously shown that in nephritis there is an accumulation of inorganic phosphate in the blood plasma, due presumably to a failure of the kidney to excrete acid phosphate. We wished to determine, therefore, the difference, if any, in ammonia production resulting from the ingestion of acid phosphate and hydrochloric acid in equimolecular amounts.

The subjects were four normal men. Each was on his usual diet throughout the experiment which continued over 12 days. There was a preliminary period of three days. During the fourth day each subject drank 500 c. c. of decinormal hydrochloric acid. Following this there was a "normal" day. On the third day each subject took the equivalent of 500 c. c. of decinormal acid sodium phosphate ($NaH_2PO_4$). On the following day 1500 c. c. of decinormal acid sodium phosphate were taken by each subject. Two "normal" days followed and then each subject took a solution of sodium phosphate having a pH of $10^{-7.4}$, that is, the reaction of the body, and containing exactly the same amount of $PO_4$ as the 500 c. c. of decinormal acid phosphate. On the following day 1500 c. c. of decinormal neutral phosphate were taken. A subsequent "normal" day completed the experiment.

In the table are shown the average values for some of the important factors. From the results, it appears that hydrochloric acid administration increases distinctly the ammonia coefficient in the urine and at the same time the titratable acid increases in about the same proportion, so that the $\frac{A}{NH_3}$ ratio remains essentially unchanged. On the other hand, the administration of acid phosphate equivalent in titratable value to the hydrochloric acid led to absolutely no increase in ammonia excretion, and even three times this amount (1500 c. c.) failed to increase the excretion of ammonia. There was, however, a great increase in the titratable acid of the urine that the $\frac{A}{NH_3}$ ratio increased greatly, reaching a point corresponding to that observed by Henderson and Palmer in severe nephritic acidosis. It would appear that the presence of phosphate in the body actually inhibits the production of ammonia, since hydrochloric acid alone leads to a great increase and the administration of 500 c. c. of decinormal acid phosphate is essentially the same (except for inert sodium chloride) as the administration

| | Vol. in c.c. | pH | A* | $NH_3$* | $\frac{A}{NH_3}$ | TN gms. | P gms. |
|---|---|---|---|---|---|---|---|
| Normal | 1570 | 6.15 | 262 | 381 | 0.68 | 13.5 | 0.98 |
| Normal | 2100 | 6.4 | 279 | 386 | 0.71 | 13.2 | 1.06 |
| Normal | 1250 | 5.9 | 328 | 380 | 0.86 | 13.7 | 1.08 |
| 500 c.c., $\frac{N}{10}$ HCl | 1860 | 5.5 | 404 | 529 | 0.76 | 13.5 | 1.05 |
| Normal | 1410 | 5.8 | 310 | 437 | 0.71 | 12.7 | .98 |
| 500 c.c., $\frac{N}{10}$ Acid Phos. | 1890 | 6.05 | 476 | 422 | 1.13 | 14.7 | 1.98 |
| 1500 c.c., $\frac{N}{10}$ Acid Phos. | 2400 | 5.8 | 956 | 439 | 2.17 | 13.3 | 3.91 |
| Normal | 1570 | 5.85 | 512 | 433 | 1.19 | 12.4 | 1.88 |
| Normal | 1130 | 6.1 | 273 | 358 | 0.76 | 11.8 | 1.11 |
| 500 c.c., $\frac{N}{10}$ Neut. Phos. | 1660 | 6.5 | 367 | 319 | 1.14 | 11.5 | 2.03 |
| 1500 c.c., $\frac{N}{10}$ Neut. Phos. | 1690 | 6.8 | 323 | 238 | 1.36 | 12.9 | 3.65 |
| Normal | 1860 | 6.7 | 295 | 319 | 0.93 | 12.4 | 1.81 |

*A represents the total titratable acid for 24 hours and $NH_3$ the total urinary ammonia, each expressed in c.c. of decinormal solution.

of an equivalent amount of neutral phosphate to which 500 c. c. of decinormal hydrochloric acid has been added. We should suppose, then, that the administration of phosphate at exactly the reaction of the body should decrease the ammonia excretion of the normal person and our results show this to be the case. There was a decrease in the excretion of ammonia after taking neutral phosphate and the $\frac{A}{NH_3}$ ratio became greater than that seen in the normal person.

The experiments reported show that the presence of acid phosphate in the body, even in the absence of renal disease, gives rise to the excretion of urine of a character such as has been previously observed only in nephritic acidosis. It is our opinion that these results give additional confirmation to the view that the acidosis occurring in the course of nephritis is due to the retention of acid phosphate.

## THE EFFECT OF ALKALI AND MALT PREPARATIONS UPON THE RETENTION OF CALCIUM IN INFANCY

By AKIRA SATO, M. D.

*(From the Harriet Lane Home and from the Department of Pediatrics, The Johns Hopkins University)*

This investigation was undertaken to see if an alkali has any beneficial influence upon the retention of calcium in an infant (as Dubois and Stolte (1913) reported in their article) and if carbohydrate has an unfavorable effect upon calcium storage, as some authors believe. Eight experiments were made upon the same infant with the same amount of milk as the diet. In some periods, sodium bicarbonate was added and in others, preparations of malt both with and without the alkali. The results were as follows:

The addition of an alkali produced not only no favorable effect upon the retention of calcium, but a distinctly unfavorable one, whereas malt extract alone without alkali acted beneficially upon calcium storage. Malt extract with a considerable amount of alkali produced a rather unfavorable result. It was therefore concluded that, if malt soup has a favorable effect upon calcium metabolism, it is not as a result of the alkali originally contained in it or added to it.

## A RAPID MICRO-METHOD FOR THE DETERMINATION OF PHOSPHATE AND TOTAL PHOSPHORUS IN URINE AND STOOLS

By AKIRA SATO, M. D.

*(From the Department of Pediatrics of The Johns Hopkins University)*

The method is a colorimetric one and depends upon the precipitation of phosphate by uranium. The precipitated phosphate is dissolved in acid and the color, developed by the addition of potassium ferrocyanide, is compared with that produced by the same reagent with a standard uranium phosphate solution. For the determination 0.5 mgm. of $P_2O_5$ is sufficient. Thus with the urine of the adult one would use 0.5 to 0.75 1 c. c., with the bottle-fed infant about 0.5 c. c. and with the breast-fed infant 5 c. c. But in each case a very simple test described in the original article should be made in order to determine the optimum amount of urine for the determination. The total phosphorus in the stools is determined in a similar way after digesting with sulphuric and nitric acids. In the analysis of theoretical solutions, the amount of inorganic phosphate was determined with an average error not exceeding 2 per cent. In that of urine and feces the method has yielded results differing by not more than 2 per cent from those obtained by the ordinary gravimetric method.

## AN UNUSUAL COMBINATION OF CARDIAC ARRHYTHMIA WITH ATRIAL ORIGIN OCCURRING IN A PATIENT WITH FOCAL INFECTION AND THYROID ADENOMATA

By LEWELLYS F. BARKER, M. D., and HENRY B. RICHARDSON, M. D.

**(To be published in full in The Archives of Internal Medicine)**

The paper describes a patient, aged 51, who for three or four years had presented nervous symptoms (insomnia, depression, weakness) and circulatory symptoms (dyspnœa on exertion, tachycardia, palpitation).

On physical examination he showed slight cyanosis, tachycardia, slight hypertension—blood pressure 145 systolic, 80 diastolic—eye signs of hyperthyroidism, oral sepsis, slight nodular struma, palpable liver, undescended left testicle. The blood was normal, the Wasserman reaction was negative, the stomach juice was normal, the urine showed a faint trace of albumin, but no casts. On X-ray examination there was slight clouding of the right antrum. Teleröntgenogram measurements: M. R. 6.7, M. L. 9.1. The adrenalin test showed rather marked hypersensitiveness to this substance. There was chronic tonsillitis and a moderate degree of benign prostatic hypertrophy without residual urine.

Electrocardiagraphic studies showed, at one time or another, the following: (1) Physiological rhythm; (2) dislocation of the pacemaker from the sino-atrial node to points elsewhere in the atrium; (3) alternate atrial extrasystoles, none of which provokes a ventricular response; (4) alternate atrial extrasystoles, many of which provoke a ventricular response; (5) paroxysmal tachycardia; (6) atrial flutter.

After removal of the oral sepsis, treatment of the paranasal sinusitis and a partial strumectomy, with general upbuilding measures, the patient markedly improved and the cardiac arrhythmia disappeared except for occasional extrasystoles. In the fuller report the bibliography is reviewed.

## A NOTE ON THE SUPPOSED RELATION OF THE SYMPATHETIC NERVES TO DECEREBRATE RIGIDITY, MUSCLE TONE AND TENDON REFLEXES

By STANLEY COBB

*(From the Department of Physiology, The Johns Hopkins Medical School and the Henry Phipps Psychiatric Clinic, The Johns Hopkins Hospital, Baltimore)*

**(To be published in the American Journal of Physiology, July, 1918)**

The question of the sympathetic innervation of striated muscle is still far from settled. As the evidence accumulates, the probability diminishes that a simple explanation of tonus has at last been found. For a time the researches in anatomy and physiology had made it seem probable that tonic muscular contraction was due to sympathetic innervation. In this work

some experiments of deBoer and Dusser de Barenne were modified and repeated. A series of experiments was done on frogs to test deBoer's observation that cutting the rami communicantes of the abdominal sympathetic in frogs causes a loss of tone in the ipsilateral leg muscles. Sixty-one frogs were operated on in different ways and although the simple cutting of the rami usually seemed to cause the leg to hang lower, no consistently corroborative evidence was obtained from stimulation or degeneration experiments. Seven cats were operated on. In one case simple unilateral excision of part of the abdominal sympathetic chain was performed; the abdominal sympathetic was cut before decerebration in five cases, and afterwards in one case. The effect of stimulating the sympathetic chain was tried out, also the effect of inhibiting decerebrate rigidity by cerebellar stimulation, with and without an intact sympathetic chain. Besides this, repeated observations were made on six cats, after their recovery from the sympathetic excision, to see if the muscular tonicity or tendon reflexes had been affected.

The following conclusions were reached:

(1) Section of the abdominal sympathetic chain in cats:
   (a) Has no effect on decerebrate rigidity, either by preventing its development or its inhibition.
   (b) Causes no obvious hypotonicity of the hind legs or tail.
   (c) Causes no change in the tendon reflexes.

(2) Stimulation of the abdominal sympathetic chain causes no tonic contraction of the ipsilateral hind leg.

# NOTES ON NEW BOOKS.

*History of Medicine, Suggestions for Study and Bibliographic Data.* By FIELDING H. GARRISON, A. B., M. D., Principal Assistant Librarian, Surgeon General's Office, Washington, D. C. Second edition revised and enlarged. Octavo of 905 pages with many portraits. (*Philadelphia and London: W. B. Saunders Company, 1917.*)

The appearance of the second edition of Garrison's work is an index of the increased interest which has been aroused in the United States in the study of medical history. The first edition was a distinct advance on previous histories of medicine in the English language, and served a most useful purpose here and elsewhere. The additions and changes in the second edition bear remarkable testimony to the zeal, scholarship and industry of the accomplished author. The work has been revised, enlarged and made even more useful to the student of history than before. It deserves the widest circulation and the most careful consideration on the part of all persons who take any interest in the checkered past of medicine, or who are stimulated by the review to cherish hopes for the future. The book is admirably printed, and the proof reading has been excellent. H.

*Syphilis.* By LLOYD THOMPSON, M. D. (*Philadelphia: Lea & Febiger, 1916.*)

The subject of syphilis is perhaps the most important one of all the great divisions in medicine to-day. As the author of the book aptly states this in the opening sentences of the preface, one must involuntarily agree with him; because, after all, some of the most brilliant researches and solutions of medical problems have been made by workers in this field in the past 15 years. Many of these conclusions, coupled with a more intensive study of the subject, have made us all so much more keenly alive and sensitive to this great problem that a book of this character can of a certainty lay a claim to some kind of recognition.

Books dealing with syphilis have always been available, varying from the chapter in the average text-book, devoted to syphilitic manifestations of the special field under consideration, up to the large systems which are, of course, encyclopedic in character. However, there is always a place for an up-to-date book which is concise, brief and yet sufficiently comprehensive to make it a thing for ready and satisfying reference.

This book should appeal particularly to the student because it deals quite broadly with the entire subject; and as stated, is certainly handy for reference for the busy teacher. It is very commendable that the author has given a decidedly interesting though necessarily brief history of the disease, and of the advancement of our present-day knowledge of it; and that he has added an interesting chapter on the importance of syphilis is a genuine advantage.

In one sense the book is encyclopedic in character, even though the discussions are not entirely comprehensive; but its very brevity in this respect is perhaps a real asset. The last part (III) devotes nearly 40 pages to a description and treatment of congenital syphilis—much of which is of necessity a repetition of what has gone before.

Among some of the noticeable features to which attention might be directed are the persistent references to the great importance of the Wassermann blood test—a factor which is, of course, of inestimable value, but which, if emphasized too much, might tend to discredit and to discourage a keener study of the clinical aspects of the disease—the very thing which permitted such men as John Hunter, Ricord, Fournier, Erb, Jonathan Hutchinson, etc., to become the great masters. We must never relax our clinical vigilance with a subject such as this, and should rely on laboratory tests rather as adjuvants.

There are a few minor defects in the text, such as typographical errors, in the misspelling of proper names and of drugs (asperin for aspirin), as well as in the use of terms (tubercular for tuberculous). However, the book has the decided advantage of bringing together in one volume all phases and aspects of the subject in proper co-ordination and good arrangement. Furthermore, it supplies what we consider an important essential for a text-book, namely, brief but significant additions culled from the author's personal experience.

Without taking up the various chapters, we would mention merely the excellent and clear expositions of laboratory technique; the helpful and not too numerous references as foot-notes; and the splendid, comprehensive, yet concise descriptions on pathology, especially of the skin manifestations.

The book is attractively presented, in very handy form; the photographs of the skin lesions are adequate but not unusual, and on the whole the book should become a necessary part of every medical student's library.

With the rapid advancement in our knowledge of syphilis of the nervous system, the appearance of the book is very timely. Much has been accomplished, especially in the matter of treatment, since the publication of this volume. The treatment of these manifestations is at present passing through a stage of trial, and judging from results published by various authors much is to be hoped for.

We, therefore, look forward to the appearance of a subsequent edition of this book with much anticipation and assurance.

I. R. P.

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